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THYROXINE THERAPY IN PREVENTIVE GERIATRICS*

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The recognition of certain discrepancies between the level of basal metabolism and the clinical picture, and the availability of a method for determining thyroxine in blood, permit a re-evaluation of the importance of thyroxine therapy in older people.

The development by Chaney (1), and later by Barker (2), of a reliable and economical method for measuring the concentration of serum protein-bound (thyroxine) iodine allows the direct assay of thyroid hormone in the circulating blood. Results of serum protein-bound iodine (PBI) determination suggest the following classification of thyroid disorders:

		PBI (μg./100 ml.)
Myxedema	Very low	(0.0–2.0)
Severe hypothyroidism	Low	(2.0–3.0)
Moderate—often pituitary—hypothyroidism	Subnormal	(3.0–4.0)
Possible hypothyroidism	Low normal	(4.0–5.0)
Euthyroidism	Normal	(5.0–7.0)
Possible hyperthyroidism	High normal	(7.0–8.0)
Hyperthyroidism	High	(8.0 & over)

Revolutionary changes have occurred in the pharmaceutical production of thyroxine, long recognized as the thyroid hormone. In 1950, Hart and MacLagan (3) reported the successful oral treatment of myxedema with a mono-isomeric synthetic levo-thyroxine. This followed twenty-five years of experience with synthetic thyroxine, usually in the racemic form. The metabolic effects of synthetic thyroxine, orally and intravenously, were studied in great detail by Thompson *et al.* in 1933–34 (4, 5, 6) but this medication did not come into general use. Chemical methods now available allow the production of pure sodium-levo-thyroxine from amino acids and iodide, at a cost comparable to that of the manufacture of crude desiccated thyroid. Taken together, the blood thyroxine method for demonstrating degrees of thyroid deficiency and the availability of

* Presented at the Annual Meeting of the American Geriatrics Society, San Francisco, California, June 17–19, 1954.

the chemically pure thyroid hormone for oral medication, provide a new approach to the diagnosis and treatment of hypothyroidism.

THE THYROID HORMONE IN GERIATRICS

The discovery and correction of subclinical hypothyroidism as a field for preventive geriatrics raises fundamental questions of biochemistry, physiology and ontogeny. The subject has already been discussed by Kimble and Stieglitz (7).

When evaluating the part played by the thyroid in the health of older people, it may be wise to start with the extreme possibility that it is of no use at all. Arthur Hertzler (8) is said to have stated that the thyroid gland is not needed by the human economy after the age of 50. To quote him directly: "Experience has tended to more and more radical operation culminating in complete thyroidectomies in certain selected cases. Myxedema has not resulted."

We now believe that Hertzler's failure to produce myxedema was due to the surgical impossibility of complete thyroidectomy; but for many years it was believed and taught that myxedema did not follow the total surgical ablation of the thyroid in dogs. The recent use of radioactive iodine in tests and in treatment has explained the absence of myxedema by showing the presence of remnants of thyroid tissue. In dogs total ablation of the thyroid does produce myxedema (9), and this is also the case in the aged human. The earlier conclusion that in old age we do not need thyroxine in our tissues is specious.

Conceivably, the amount of hormone needed by the tissues of the aged may be less than that needed by the tissues of the young. If the concentration of thyroid hormone in the cells of healthy humans of great age is the same as when they were younger, the maintenance of this level may be necessary for longevity, and either an excess or an insufficiency may shorten life. The problem may be stated in another way: if health and longevity are associated with a slowing down of chemical reactions, it may be best to have a gradual reduction of thyroid hormone in the tissues; but if the rate of chemical reactions remains unchanged, the hormone concentration should remain the same.

In Figure 1 data are presented which show the relationship between the serum protein-bound iodine level and the age of the subject. In a group of 28 patients, without evidence of thyroid disease, who were 75 years of age or more, the mean value for PBI was found to be 5.2 micrograms per 100 ml. The normal control value for young adults in this laboratory is 5.57.

Dailey (10) determined the concentration of protein-bound iodine in the serum of 309 patients from 10 to 80 years of age, who had normal thyroid function. The group excluded all patients who had undergone thyroid surgery, and all cases of exogenous obesity, goiter, thyroid medication, or any glandular dysfunction; but it included a miscellany of diseases such as carcinomatosis, leukemia, arthritis and anxiety states. There is no correlation in this graph between age and protein-bound iodine level (Fig. 2).

A similar datum is the measurement of thyroid activity by the uptake of radioactive iodine. Quimby, Werner and Schmidt (11) made a large number of determinations of the 24-hour uptake of radioactive iodine in normal human

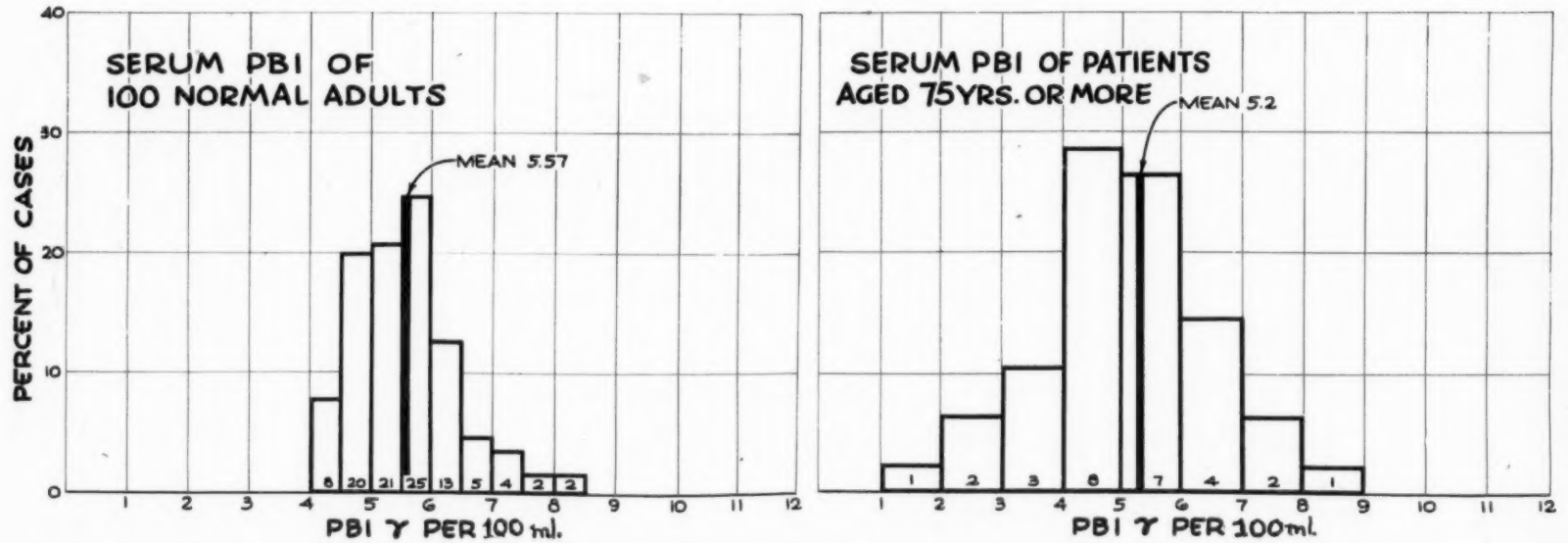
SERUM PBI OF
100 NORMAL ADULTS
MEAN 5.57
PERCENT OF CASES
PBI γ PER 100 ml.
8 20 21 25 13 5 4 2 2
SERUM PBI OF PATIENTS
AGED 75YRS. OR MORE
MEAN 5.2
PBI γ PER 100ml.
1 2 3 8 7 4 2 1

FIG. 1. Comparison of mean serum protein-bound iodine level of young adults with that found in 28 patients 75 years of age or more. The small numbers at the bases of the columns indicate the number of individuals in each group. Note that there are no cases of hypothyroidism (PBI, 0–4 γ) in the adult group, as compared to 6 cases (about 25 per cent) in the aged group.

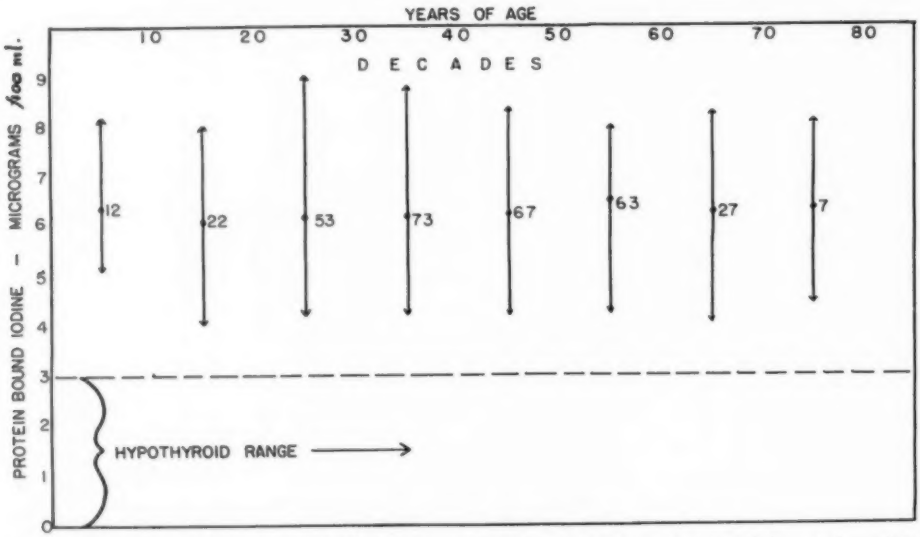

FIG. 2. Serum protein-bound iodine determinations in 309 patients without thyroid disease, from youth to old age. (Courtesy Doctor M. E. Dailey, Medical Center, University of California.)

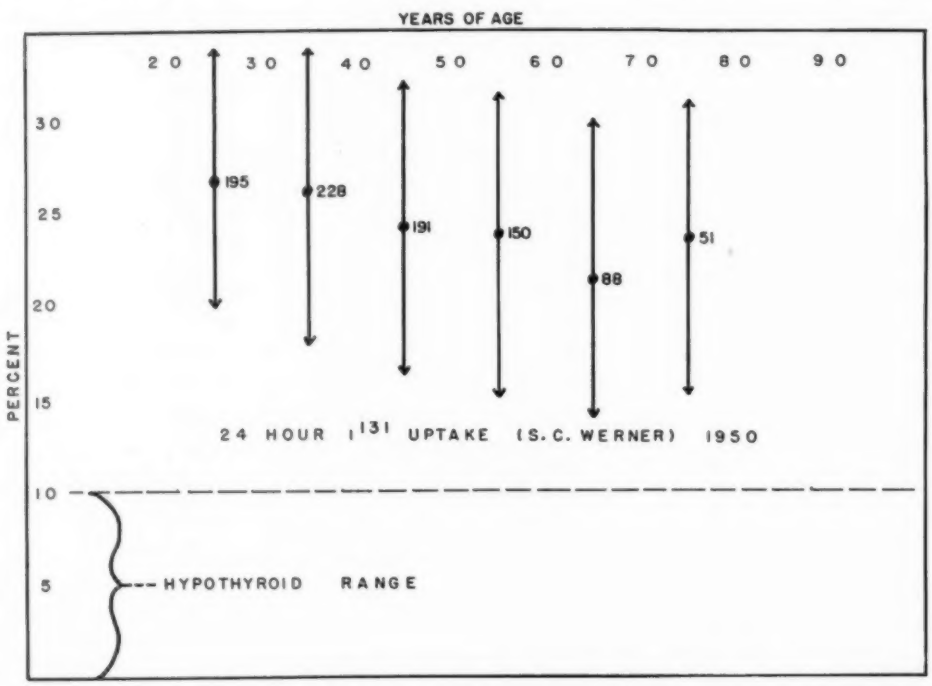

FIG. 3. The 24-hour thyroidal uptake of radioactive iodine in normal subjects, by decades of life. Note hypothyroid range. (Reproduced with permission from Quimby, E. H.; Werner, S. C., and Schmidt, C.: *Proc. Soc. Exper. Biol. & Med.* **75:** 537, 1950.)

beings, tabulated by age (Fig. 3). This demonstrates that there is no significant decrease of uptake with advancing years.

In classic studies, the basal metabolic rate has been assumed to decline in the older age groups. A gradual decline from 39.5 calories per square meter per hour,

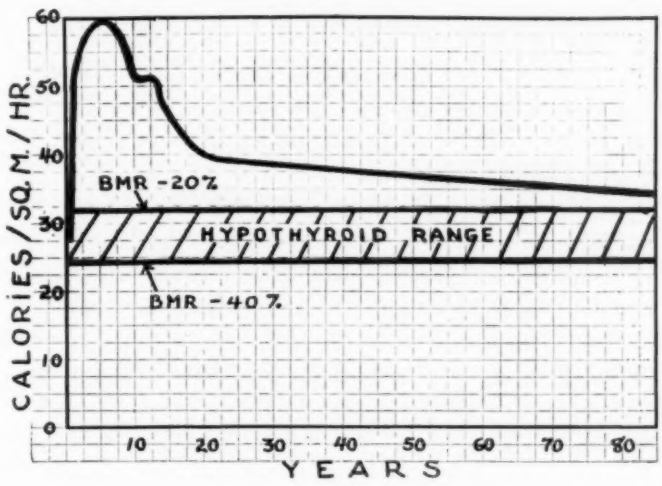

FIG. 4. Basal metabolism in terms of calories per square meter per hour (men) by decades. Range of hypothyroid values for twenty-year standard is −20 to −40 per cent. Note that the normal metabolic rate at 85 years of age is still well above this hypothyroid range. (Based on Aub-Dubois data in "Basal Metabolism in Health and Disease." Philadelphia, Lea & Febiger, 1936.)

characteristic of the two decades from 20 to 40 years of age, begins in the fifth decade, decreasing by one calory per square meter per hour for each subsequent decade. In the eighth decade the value is 35.5; that is, at 80 years of age the value is 4.0 units lower than the value at 40 years (12). Thus there is at the extremity of life only slightly more than a 10 per cent reduction from the basal energy level required at the chronologic mid-point of life (Fig. 4).

Some attention may be given at this point to the lack of homogeneity of the human race. Benedict and Meyer (13) found a scatter ranging from +15 to −24 per cent in the basal metabolic rates of 23 normal women from 66 to 86 years of age. In a small group of men studied by Benedict and Root the rates ranged from −31 to +5 per cent. These metabolic values represent statistical averages; the dispersion of the data is considerable and no answer is given as to whether or not the maintenance of the basal metabolic rate within about 10 per cent of that of mid-life is desirable for health.

Indeed it may be that considerable difference in health is present in the aged group, and there is no indication of the benefit or harm of maintaining the metabolic rate at so nearly a normal level. Those with the higher rates may be burned out, like an old automobile engine, and those with the lower rates in this same group may be running more efficiently. The opposite may be true; those with greater heat production may have more normal biochemical processes than those with lower heat production.

When the basal metabolic rate was commonly believed to represent the level of a patient's thyroid function, this tenet—the fall with age—was taken to indicate hypothyroidism in older persons. Now that the direct measurement of circulating thyroid hormone (serum protein-bound iodine: Taurog and Chaikoff (14)) is found to provide a good indication of tissue activity, it must be con-

cluded from the evidence that the aged have a normal concentration of thyroid hormone in their tissues. The basal metabolic rate is probably low in some old people, but whether these people are healthy or not remains to be determined. Their lower rate of oxygen consumption may be due to lessened somatic muscle mass or to other similar factors.

The heat production of the body measured indirectly by the oxygen consumption, *i.e.*, the basal metabolic rate, is only 10 per cent less in late life than in middle life. In the athyreotic patient, then, the maintenance of basal heat production would require approximately the same dose of exogenous thyroid hormone. There probably is, however, a decrease in the total heat production by the aged because of such factors as reduced muscular activity, so that the total daily dose of thyroid medication required may be less. Adequate data on this point are not available. The occurrence of myxedema late in life, however, should be a point in favor of the argument that thyroxine is necessary for the tissues. The serum protein-bound iodine values, and the dosages of thyroid and thyroxine in 11 patients with senile myxedema are given in Table 1.

If hypothyroidism were related only to youthful demands, *i.e.*, occurred because metabolic and dynamic energy requirements were relatively too high in earlier years, it is possible that one might outgrow the need for exogenous thyroid medication. Thus one might reach a stage of life so extended that rapid heat production would not be needed. This does not seem to be true. G. R. Murray, in the British Medical Journal of 1920, reported the life history of the first case of

TABLE 1

Patient	Age	Initial serum PBI (μg./100 ml.)	BMR (%)	Thyroidal I uptake (%)	Maintenance dose
L. N.	78	1.3	—	0	Desiccated thyroid, 1 grain daily
M. A.	74	1.2	—	7.1	
B. M.	74	2.5	−22	—	Desiccated thyroid, 1 grain daily
B. W.	73	1.6	−34	—	Desiccated thyroid, 1 grain daily
G. H.	72	1.7	—	4.3	
R. B.	70+	3.4	−9	—	Sodium-levo-thyroxine*, 0.4 milligram
M. T.	72	0.8	—	3.7	Sodium-levo-thyroxine, 0.2 milligram
M. M.	78	(on desiccated thyroid) 3.2	—	(on desiccated thyroid) 12%	Sodium-levo-thyroxine, 0.1 milligram
A. A.	70+	1.5	—	2.9	Sodium-levo-thyroxine, 0.2 milligram
B. G.	74	(on desiccated thyroid) 2.9	—	—	Sodium-levo-thyroxine, 0.2 milligram
E. M.	75	1.4	—	4.7	Sodium-levo-thyroxine, 0.3 milligram

* See text footnote 1.

myxedema treated with thyroid. This patient began treatment in 1891 at the age of 46 and died in 1919 at the age of 74. The need for the hormone continued in the later years.

Through the courtesy of Dr. S. Gordon Ross, I am privileged to mention a still more remarkable patient—a woman now approaching her ninety-seventh birthday, in whom myxedema developed in 1882 when she was 25 years of age. She remained in this state until 1894, when she was 37 years old. Thyroid therapy was then started and she is still taking 1½ grains of desiccated thyroid daily. Discontinuance of the medication in the past, on doctor's orders, has led to a fall in basal metabolic rate from −5 to −35 per cent.

One may conclude then that the need for thyroxine continues without much change in amount, throughout life. Can one conceive that this patient at the age of 97 has actually lived longer than if she had to depend on her own thyroid gland for thyroxine?

The debilitating effects of hypothyroidism are well recognized. It seems highly probable that excessive and early atherosclerosis with its attendant morbidity and mortality may be the result of prolonged hypothyroidism (15).

That hypothyroidism may exist in a subclinical state without pathognomic symptomatology has been emphasized in one of our previous publications (16). The following case is an example:

Mr. H. J. was a 46-year-old newspaper photographer, who was first seen by us on February 21, 1952, because he wished a check-up to exclude cancer of the stomach. His eating habits were very irregular. His gastrointestinal symptom was nausea, but there were no other stomach and bowel symptoms, except for a single loose stool with flatus after a normal daily bowel movement. Some respiratory difficulty was thought by the patient to be asthma. He showed signs of nervous tension and anxiety. His eyes were swollen and lacrimating. There was not much in the clinical picture to suggest myxedema.

On physical examination the blood pressure was 100/70 and the pulse was 60. Carotid sinus pressure produced cardiac arrest. He had a congenitally ichthyotic skin. The heart was quiet and the abdomen normal. The prostate was of normal size. Again, there was little suggestion of myxedema.

The laboratory data were as follows:

Hemoglobin	15.5 grams per 100 ml.
White blood cells	9,000 per cu.mm.
Erythrocyte sedimentation rate	2½ mm./min.
Urine: specific gravity	1.018
pH	6.0
Albumin	0
Sugar	0
Microscopic	0
Blood sugar	108 mg./100 ml.
Electrocardiogram	Flat T waves
Serum protein-bound iodine	2.3 micrograms per 100 ml.
Repeated	2.8 micrograms per 100 ml.
Serum cholesterol	300 mg. per 100 ml.
Basal metabolic rate (unsatisfactory)	±0 per cent; pulse 60–64

The diagnosis of severe hypothyroidism was established by the consecutive serum protein-bound iodine determinations of 2.3 and 2.8 micrograms per 100 ml.

Treatment: On April 3, 1952, sodium-L-thyroxine[1] was started in a daily dosage of 0.2 milligram by mouth. On May 27 the electrocardiogram showed normal T waves. The value for serum protein-bound iodine was 5.1 micrograms per 100 ml., and for serum cholesterol, 190 milligrams per 100 ml. On July 25 the level of serum protein-bound iodine was 4.2 micrograms per 100 ml., and of serum cholesterol, 220 milligrams per 100 ml. The dosage of sodium L-thyroxine was increased to 0.4 milligram daily. On September 23 the value for serum protein-bound iodine was 4.4 micrograms per 100 ml., and for serum cholesterol, 215 milligrams per 100 ml. The dosage of sodium-L-thyroxine was increased to 0.5 milligram daily. On September 29, 1952, the serum protein-bound iodine level was 5.7 micrograms per 100 ml. On January 26, 1953, it was 6.4 micrograms and the serum cholesterol level was 202 milligrams per 100 ml. The dosage of sodium-L-thyroxine was continued at 0.5 milligram daily.

This patient seems to be well maintained by 0.5 milligram of oral sodium-L-thyroxine daily, and he probably will continue this medication, with proper encouragement, for the remaining thirty or more years of his life. It is possible that, if the diagnosis of hypothyroidism had not been made, his life would have been shortened by the effects of thyroid deficiency.

Thus, thyroid gland failure may be a common occurrence in the later decades of life, similar in pattern to ovarian failure, which regularly produces the menopause. However, the deficiency of thyroid hormone is productive of a pathologic condition that shortens life. This is also true of postmenopausal, uncompensated hypo-ovarianism. It is recommended that serum protein-bound iodine determinations be used as a regular screening process in all middle-aged patients. If a subnormal value is found, substitution therapy with oral sodium-levo-thyroxine should be instituted and maintained throughout the rest of the patient's life. The finding of a serum protein-bound iodine value below 4.0 micrograms per 100 ml. is an indication for thyroid medication.

SUMMARY

The problem may be stated as follows: 1. Does health in the later years of human life depend, among other things, upon maintenance of the same concentration of thyroxine in the tissues as is needed for health in young adults? The evidence derived from determinations of serum protein-bound iodine and thyroidal uptake of radioactive iodine suggests an answer in the affirmative. 2. The maintenance dosage of thyroxine necessary for health in the extremely aged would seem to be of the same order of magnitude as that necessary for the maintenance of hypothyroid patients in middle life. 3. The dosage requirement of a described athyreotic patient has not decreased significantly in a period of sixty years. This patient, now 97 years old, has been receiving thyroid medication since 1894. 4. It seems highly probable, although not exclusively demonstrated, that atherosclerosis and other degenerative diseases may be associated with hypothyroidism, with the result that life is shortened. 5. Certain possible discrepancies between the basal metabolic rate and the clinical condition should be kept in mind when appraising thyroid function. 6. Subclinical hypothyroidism

[1] Sodium-levo-thyroxine (Synthroid, Travenol) provided by the generosity of Dr. Robert P. Herwick of Baxter Laboratories, Inc., Morton Grove, Illinois.

may be discovered by the use of the serum protein-bound iodine (circulating thyroxine) determination. 7. Maintenance of adequate circulation of thyroxine to the tissues for extended periods may be obtained by the oral ingestion of sodium-levo-thyroxine.

CONCLUSION

Old people are not normally hypothyroid; middle-aged people should not be allowed to become hypothyroid.

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ANTICOAGULANT THERAPY IN FRESH INFARCTION OF THE HEART

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Wright (1) reported favorably in June 1948 on the use of anticoagulant in the treatment of coronary thrombosis with myocardial infarction. The preliminary report of the Committee for the Evaluation of Anticoagulants organized by the American Heart Association collected the data on 800 patients from several hospitals. The series was controlled by withholding anticoagulant from patients admitted on alternate days. At that time the use of anticoagulant in such cases was made part of the routine therapeutic regimen on the medical service of the Toronto General Hospital.

This report is based on the results of analysis (2) of all patients with cardiac infarction surviving forty-eight hours of admission during the five and a half-year period, 1947 through mid-1952. The 503 attacks in 488 patients in which anticoagulants were administered were all seen in the latter four years of this period. The control group of 242 attacks in 240 patients consisted of 163 cases seen prior to adopting anticoagulant therapy and the remainder are those patients in whom, for one reason or another, anticoagulant was withheld.

METHODS

Dicumarol® was given in most of the treated attacks but in other treated cases intramuscular heparin, phenylindanedione (Danilone®), cyclocumarol (BL 5), and Tromexan® (ethyl biscoumacetate) were administered. Very few patients received a combination of anticoagulants. An attempt was made to keep the prothrombin time about double the normal (simultaneous) level. Daily prothrombin times were determined by the Quick (one-stage) method and continued until the patient became ambulatory. Anticoagulant was withheld in patients with disturbances of the clotting mechanism, peptic ulcer, significant liver damage, increased capillary fragility or cerebral infarction. When bleeding became troublesome, vitamin K_1 or K_1 oxide (500–1,000 mg., by mouth) restored the markedly increased prothrombin time to normal in a few hours.

RESULTS

The age and sex distributions along with gross mortality rates in the treated and in the control cases are shown in Table 1. The number of attacks ending fatally in each subgroup is shown by the figures in brackets. The increasing proportion of females in the older age groups as well as the higher mortality among females is apparent.

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TABLE 1*

	Age				Total	Mortality rate, %
	Under 50	50–59	60–69	70+		
Treated group (22.6% females)						
Males	88 [5]**	118 [16]	131 [17]	52 [11]	389 [49]	12.9
Females	9 [0]	27 [2]	39 [6]	39 [12]	114 [20]	17.5
Total	97 [5]	145 [18]	170 [23]	91 [23]	503 [69]	13.7
Control group (33.9% females)						
Males	25 [3]	41 [8]	54 [17]	38 [15]	160 [43]	25.6
Females	8 [1]	11 [2]	29 [10]	34 [19]	82 [32]	39.0
Total	33 [4]	52 [10]	83 [27]	72 [34]	242 [75]	31.0

* The data in this and in six of the following tables are reproduced with the permission of the publisher, from Burton, C. R.: Anticoagulant therapy of recent cardiac infarction, *Canad. M. A. J.* **70:** 404, 1954.

** Figures in brackets denote number of attacks ending fatally.

TABLE 2

	Mortality rate		Thromboembolism	
	Treated	Control	Treated	Control
	%	%	%	%
Mills (Canada) (3)	13.0	23.4	9.0	18.0
Wright (United States) (1)	16.0	23.4	10.9	26.0
Gilchrist (Britain) (4)	16.2	30.6	9.0	21.8
Present series (2)	13.7	31.0	12.7	22.0

Table 2 shows the results reported in other large controlled series (1–4). There was a significant reduction in the mortality rate from 31.0 per cent in the 242 control patients to 13.7 per cent in the 503 anticoagulant-treated patients. However, the probability of death from coronary thrombosis is materially influenced by age, sex, angina, previous infarction and pre-existing hypertension (5). Analysis shows that the control and treated groups were not strictly comparable with regard to these factors.

Age: The average age of the control patients was 63 years; and of the treated patients, 58 years.

Sex: Females comprised 34 per cent of the controls and 22.6 per cent of the treated patients.

Previous infarction was noted in 26 per cent of the controls and in 24 per cent of the treated patients. As seen in Table 3, the mortality rate in initial attacks fell from 28 per cent in the controls to 12 per cent in treated patients; and that in multiple attacks fell from 40 per cent in the controls to 19 per cent in patients under treatment.

Angina. The mortality rate was reduced from 28 per cent in 69 controls to 18 per cent in 149 treated cases.

TABLE 3. *Influence of Multiple Infarctions on the Mortality Rate*

	Treated	Controls
Number of initial attacks	382	177
Number of multiple attacks	121 (24%)	63 (26%)
Mortality		
In initial attacks	(47 in 382) 12%	(50 in 177) 28%
In multiple attacks	(23 in 121) 19%	(25 in 63) 40%

TABLE 4. *Effect of Angina and Hypertension on the Mortality Rate*

	503 Treated			242 Controls		
	No.	Deaths	Mortality rate	No.	Deaths	Mortality rate
			%			%
Hypertension and/or angina	189	39	21	91	25	27
Neither hypertension nor angina	314	30	9.5	151	50	33

Hypertension. The mortality rate was 27 per cent in 34 controls and 24 per cent in 63 treated cases.

In Table 4, mortality rates in patients with hypertension and/or angina are contrasted with those exhibiting neither. In the former, mortality dropped from 27 per cent to 21 per cent with treatment, and in the latter from 33 per cent to 9.5 per cent. It would seem that anticoagulant therapy exerts its greatest benefit when neither angina nor hypertension exists, probably because of the considerable reduction in thromboembolic phenomena.

There was no significant difference between the two groups in the incidence of *diabetes mellitus* or in the anatomic *site of infarction* in the heart as determined electrocardiographically.

The incidence of *thromboembolic phenomena* in the control and in the treated groups is illustrated in Table 5. Clinically significant thromboembolic episodes

TABLE 5. *Thromboembolic Phenomena*

Site	Control group	Treated group	
		All	Adequate anticoagulant
	%	%	%
Recurrent cardiac pain	10.0	5.3	2.0
Further cardiac infarction	3.3	0.4	
Pulmonary embolism	8.0	3.0	0.6
Cerebral infarction	5.4	2.4	1.2
Peripheral embolism	3.7	2.4	0.4
Venous thrombosis	2.0	1.0	0
Total	22.0	12.7	3.2

occurred in 22 per cent of attacks in controls. Although such episodes occurred in 12.7 per cent of treated attacks, in only 3.2 per cent of treated cases was the patient under the influence of adequate anticoagulant at the time; in the other 9.5 per cent the episode occurred, 1) before anticoagulant was started, 2) before it had time to assert its influence, or 3) when its influence was inadequate because of carelessness or difficulty in maintaining sufficiently increased prothrombin times.

TABLE 6. *Hemorrhagic Complications in 5 per cent of 503 Cases Treated with Anticoagulants*

Intracranial	4 (cause of death in 2)
Hematuria (gross) (prothrombin % excessively low in 7)	12
Hematemesis (from silent peptic ulcer)	1
Blood in stool (prothrombin % excessively low in 4)	5 (transfusion in 1)
Subcutaneous hematomas	2
Hemarthrosis	1
Hemorrhage into subpleural bleb	1

TABLE 7. *Causes of Death*

Cause of death	503 Treated	242 Controls
1. *Cardiac*	*62* (*90%*)	*55* (*75%*)
Recurrent pain	7	4
Sudden death	20	14
Failure	32	35
Heart block	1	1
Ventricular tachycardia	—	1
Ruptured septum	2	—
2. *Thromboembolism*	*5* (*7.5%*)	*19* (*25%*)
Pulmonary embolism	1	2
Cerebral infarction	1	9
Mesenteric embolism	—	2
Renal embolism	—	1
Embolism to bifurcation of aorta	1	2
Multiple embolism	2	3
3. *Hemorrhage*	*2*	*0*
4. *Other*	*0*	*1*
Total	69 (13.7%)	75 (31.0%)

TABLE 8. *Necropsy Findings*

	503 Treated	242 Controls
Number of necropsies	30	39
Mural thrombus	13 (43%)	27 (69%)
Embolism total	3 (10%)	24 (62%)
Embolism clinically apparent	2	12
Hemorrhage	5 (cause of death in 1)	4
Rupture of myocardium	4	0

TABLE 9. *Analysis of Series by Method of Russek*

	500 Treated	242 Controls
"Good risk"	156 (31%)	58 (24%)
Deaths	3 (2%)	3 (5%)
Thromboembolism	6%	11.5%
"Poor risk"	344 (69%)	184 (76%)
Deaths	66 (19%)	71 (40%)
Thromboembolism	15%	24%

Hemorrhagic complications occurred in 5 per cent of anticoagulant-treated patients. There were 2 deaths, both from intracranial hemorrhage in hypertensive individuals (Table 6). Prothrombin times were excessively increased in each. Bleeding occurred in 2 per cent of cases in the control group. Anticoagulant therapy was withheld from 6 per cent of the control group because of a history of bleeding.

As may be seen in Table 7, death due to embolism was considerably reduced from 25 per cent of the 75 deaths in the controls to 7.5 per cent of the 69 deaths in the treated patients. Thus 8 per cent of controls and 1 per cent of treated patients died of embolism. However, in only 1 of the 5 deaths from embolism in treated cases was the patient under the influence of adequate anticoagulant therapy (0.2 per cent of 503 treated attacks).

Necropsy findings of interest are given in Table 8.

Table 9 shows that when this series was analyzed according to "good" and "poor" risks on the basis of the findings of Russek *et al.* (6), the most marked reduction in mortality rate was found in the "poor risks," *e.g.*, from 40 per cent in the controls to 19 per cent in the treated group. The suppression of thromboembolism was apparent in both "good" and "poor" risks.

CONCLUSIONS

Patients with recent cardiac infarction, given anticoagulant in addition to the usual regimen of treatment, show a significant reduction in mortality rate and incidence of thromboembolism. Hemorrhage is not a serious threat when the patient is under ideal hospital conditions of adequate daily control.

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USE OF PSYCHOLOGIC TESTS IN DETERMINING PROGNOSIS AND TREATMENT IN GERIATRIC MENTAL ILLNESSES*

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In 1949 we began a study to ascertain if psychologic tests could be made of greater clinical value, particularly in determining the prognosis and treatment of psychiatric patients. After considering eleven tests, we designated the following three as the standard: The Wechsler-Bellevue intelligence test, the Minnesota multiphasic personality inventory (MMPI) and the Rorschach test. During the four years beginning in 1949, 7,000 psychologic tests were made—in serial and progress form, whenever possible. Ten per cent of the tests were made on patients aged 60 years or older, and it is this group with which this report is primarily concerned.

The objectives of the study were: 1) to obtain more insight into the individual patient's problem so that sounder prognosis might be made and treatment determined, 2) to provide an aid, through follow-up tests, in evaluating the patient's progress, and 3) to have tangible material for reference in supplementing an opinion when discussing the patient's needs with relatives. Our findings were of particular value in the case of geriatric patients with a psychosis. Previous to the use of insulin, any person past 59 in whom mental illness developed usually died soon, or underwent prolonged hospitalization. It is still generally believed that geriatric mental illnesses are caused solely by brain atrophy or arteriosclerosis, and therefore the situation is hopeless. In textbooks, the sections on mental illness still foster the poor prognosis. This presumption is not entirely valid. In our personal experience (1) modern therapy has helped many psychiatric oldsters; and courage, patience and persistence on the part of the doctor and the relatives have been vital factors in obtaining maximum results. It has been shown (2) that even elderly persons with cerebral atrophy or arteriosclerosis may respond to modern therapy, and the rapidly increasing number of older people stresses the need for better understanding and treatment of that group.

MATERIAL AND METHODS

During this study 141 geriatric patients with mental illnesses were given a total of 700 psychologic tests. The diagnosis in all the patients tested, before we saw them, had been senile dementia. In the group were 59 males and 82 females, in age groups as follows: 63 aged 60–64; 40 aged 65–69; 26 aged 70–74; 7 aged 75–79; and 5 aged 80–85. The average age of the group was 68 years. Those seen

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in the first six months of illness were considered in the acute, or A stage; those seen in the second six months were considered in the subacute, or B stage; and those seen after twelve months were considered in the chronic, or C stage. The treatment results were rated as: 1) occupational, excellent recovery or remission (return to normal activity), 2) social recovery or remission (home life without particular assistance and need of attention) and 3) no improvement. In considering data from the psychologic tests, it was deemed advisable to limit and group the information. Only the full scale I.Q. of the Wechsler-Bellevue test was used in our general consideration. In the MMPI of the aged, the interest (Mf) and hypomanic (Ma) items are negligible. The hypochondriasis (Hs), depression (D) and psychasthenia (Pt) categories have so much in common that they were classified as the D, or depression, trends. The hysteria (Hy), paranoid (Pa) and schizophrenic (Sc) items were classified as the Sc, or schizoid, trends. The Rorschach test responses were also classified into similar depression and schizoid trends.

CLINICAL DATA

Of the 141 patients in the study, 41 presented evidence of organic changes such as arteriosclerosis, coronary thrombosis, chronic myocarditis, chronic nephritis, chronic encephalitis and toxic goiter; or they currently had influenza, pneumonia, brain contusion, or were receiving ACTH therapy. These will be referred to as the organic group. There was no evidence of somatic disease in the other 100 patients, who will be called the functional group.

Organic group

Of the organic group, 10 patients were seen at ages ranging from 62 to 80 years (average, 71.7 years). Two were in the A stage, 2 in the B stage and 6 in the C stage. They had an average I.Q. of 70 and their deterioration was 32 per cent on the average. *Confusion* was the outstanding finding of the MMPI and Rorschach tests. Usually there was some evidence of schizoid and depression trends. The prognosis was very poor. These patients were considered to have senile dementia and permanent domicilary care was advised. The average time for hospital observation, testing and finding a rest home was thirty-five days.

The other 31 patients of the organic group fall into three classes psychologically. In the first class, the *D and the Sc elements* of the MMPI and Rorschach tests were most obvious. There were 17 in this group and their average age was 68 years. Eight were in the A stage, 2 in the B stage and 7 in the C stage. Their average I.Q. was 93 and they showed little evidence of deterioration. The prognosis was fair. The recommendation was electric-shock treatments (EST) combined with insulin-shock therapy and follow-up psychotherapy. Nine made occupational recoveries. Four of the 9 (2 A-stage, 1 B-stage and 1 C-stage) followed the recommended therapy and used an average of 15 EST. Four (A-stage) used insulin shock and psychotherapy, and 1 patient (A-stage) used psychotherapy. Five patients showed social remissions. Three followed the recommended treatment (1 B-stage and 2 C-stage) and used an average of 20 EST; 2 (C-stage) used insulin shock and psychotherapy. Three patients did not improve (1 A-stage and

2 C-stage). One used insulin shock and psychotherapy and 2 used only psychotherapy. The group that recovered spent an average of sixty-six days in the hospital and the average for the entire group was eighty-nine days. In this class, emphasis must be placed on the importance of getting the treatment started early to achieve best results. The recovery rate of 53 per cent compares favorably with that for similar illness in younger persons.

Twelve patients in the organic group showed *depression trends* as the outstanding findings in the psychologic tests. Their average age was 68 years. Six were seen in the A state, 2 in the B stage and 4 in the C stage. Their average hospital stay was forty-seven days. Their average I.Q. was 97 and they showed little evidence of deterioration. The prognosis was good. EST and psychotherapy were advised. Tonic insulin therapy was optional. Eight patients showed occupational remissions; 7 of them (3 A-stage, 1 B-stage and 3 C-stage) followed the recommended treatment and 1 (A-stage) used psychotherapy alone. Two had social remissions, 1 (B-stage) using the recommended treatment and 1 (C-stage) using psychotherapy. There were 2 failures; 1 patient (A-stage) used insulin and psychotherapy and 1 (A-stage) used psychotherapy. The patients who followed the recommended treatment received an average of 12 EST. Five of the patients in the acute, and 3 in the chronic stage made occupational recoveries. In this class, the occupational recovery rate of 66 per cent was only fair. It should be borne in mind that the co-existent organic findings made organic brain changes a possibility, even though the psychologic tests indicated otherwise.

In the third class were 2 patients with *epilepsy* of recent origin, who were seen at the ages of 63 and 69. Both showed schizoid psychologic patterns. The prognosis was poor. They were advised to use medical care, insulin therapy and psychotherapy. One in the C stage followed the recommended treatment and made an occupational recovery. The other in the B stage refused treatment and did not improve.

Functional group

Patients with psychiatric illness uncomplicated by somatic disease numbered 100. Clinically, 49 had involutional melancholia, 22 had involutional psychosis, 19 had reactive depression, 3 showed psychopathic deviations and 1 had a chronic schizophrenia.

In the 49 patients with *involutional melancholia* the average age was 66 years. Of these, 28 were in the A stage, 13 in the B stage, and 8 in the chronic or C stage. The average I.Q. was 100. The deterioration was usually slight, although it did reach 44 per cent in 1 case. The psychologic tests showed D as the predominant trend. The prognosis was good. They were advised to use EST and psychotherapy. Tonic insulin treatment was optional. This group as a whole spent an average of sixty-seven days in the hospital. The 28 patients in the A stage (average age, 65 years) spent an average of fifty-five days in the hospital. Twenty-six made occupational recoveries; 1 had a social remission and 1 showed no improvement. The latter used psychotherapy alone; the patient showing the social remission used insulin shock and psychotherapy. Of the 26 patients who reached an occupational recovery, 1 had psychotherapy alone, 4 had insulin shock and

psychotherapy and 21 had the recommended treatment. The average number of EST used was 11. There were 13 patients in the B stage; 11 reached an occupational recovery, 1 made a social remission and 1 did not improve. Their average age was 67 years and they required an average of seventy-seven days in the hospital. Of the patients who reached occupational recoveries 1 had psychotherapy, 2 had insulin shock and psychotherapy, and 8 had the recommended treatment. One social recovery and 1 failure followed the use of EST and psychotherapy. The average number of EST used was 17. The 8 patients in stage C had an average age of 69 years and spent an average of seventy-nine days in the hospital. Seven made occupational recoveries. They followed the recommended treatment and received an average of 11 EST. One used insulin shock and psychotherapy and made a social recovery. The overall results were most encouraging in this group. Forty-five of 49 patients reached occupational remissions. This compares favorably with the results of treatment of similar affective illnesses in younger persons.

The patients with uncomplicated *involutional psychosis* numbered 22. Their average age was 66 years. They spent an average of eighty-seven days in the hospital. The average I.Q. was 96 and there was little evidence of deterioration. The psychologic tests showed depression and schizoid trends predominating. The prognosis was fair. The recommended treatment was EST, insulin shock and psychotherapy. Nine of the patients were in the A stage, 3 in the B stage and 10 in the C stage of their illness. Group A had an average age of 67 years and spent an average of eighty days in the hospital. Eight of them followed the recommended treatment and reached occupational recoveries. The average number of EST used was 12. One patient (A-stage) used insulin shock therapy and psychotherapy and reached a social remission. The 3 patients in the B stage were of an average age of 64 years and spent an average of eighty-nine days in the hospital. Two of these patients used the recommended treatment and made occupational recoveries. The average number of EST used was 10. One patient had insulin shock and psychotherapy and reached a social remission. The 10 patients in the C stage had an average age of 64 years and spent an average of ninety-eight days in the hospital. Three patients followed the recommended treatment and made occupational recoveries. Three patients made social remissions following use of the recommended therapy. There were 4 failures; 1 of these patients used the recommended treatment, 2 used insulin shock and psychotherapy and 1 used psychotherapy. The patients who used the recommended therapy received an average of 13 EST. The overall recovery rate of 59 per cent in uncomplicated involutional psychosis was only 6 per cent better than the rate for similarly affected patients in the organic group.

In 19 patients the diagnosis was *reactive depression*. They had had a sudden severe depression following operation, illness or some shocking and unexpected bad news. Their average age was 66 years and they spent an average of fifty-one days in the hospital. Their average I.Q. was 94, and the deterioration percentage was slight. The psychologic tests showed depression as the predominant element. The prognosis was good. The recommended treatment was EST and psychotherapy; insulin was optional. Eight were in the A stage, 1 in the B, and 10 in

the C stage. The A group had an average age of 62 years and spent an average of sixty-three days in the hospital. Of the 8 patients in this group, 4 made excellent recoveries; 1 followed the recommended treatment and used eight EST, 2 used insulin shock and psychotherapy, and 1 used psychotherapy. Three other A-group patients made social remissions; 2 used insulin shock therapy and psychotherapy and 1 used psychotherapy. One patient did not improve following insulin shock and psychotherapy. The only patient seen in the B stage used insulin shock and psychotherapy and made an occupational recovery. The 10 patients in the C stage had an average age of 66 years and spent an average of forty-four days in the hospital. Four of them made occupational recoveries; of these, 2 used the recommended treatment and had an average of eight EST, and 2 used psychotherapy. There were 3 social remissions and 2 failures following insulin shock and psychotherapy and 1 failure following psychotherapy alone. The occupational recovery rate of 47 per cent was highly unsatisfactory. An equal number of similar situations occurring before the age 60 would have had an occupational recovery rate of nearly 100 per cent. These oldsters whose illness was initiated by real adversity had a poorer prognosis than did the depressed geriatric patients in the organic group.

The 3 patients who were classified as constitutional psychopaths had an average age of 64 years. They were all in the chronic, or C stage. Their average I.Q. was 104, and they showed marked deterioration. The average stay in the hospital was twenty-seven days. The psychologic tests showed the predominance of depression and schizoid trends plus a marked psychopathic-deviate element. The prognosis was poor. EST, insulin shock and psychotherapy were recommended. Insulin shock and psychotherapy were used in all, but all failed to improve.

The patient with chronic schizophrenia was 65 years of age and spent three hundred and thirty-two days in the hospital. Her I.Q. was 98. The prognosis was poor. She received 45 EST, and was treated for ten months with insulin shock and psychotherapy, but did not improve.

DISCUSSION

It is of interest to see how our older patients, as a group, measured up intellectually. It was not possible to administer the Wechsler-Bellevue test to all patients but a sufficiently large group (Table 1) was tested to make these figures reasonably representative of the entire group. The data in Table 1 indicate that this group was average in intelligence. This test was administered at the time the patient entered the hospital. The scores probably err in the direction of being too low.

One of the purposes of the MMPI and Rorschach tests was to measure the

TABLE 1. *Ranges and Means of Wechsler-Bellevue I.Q.*

	No. Cases	Range of I.Q.	Mean I.Q.
Verbal scale I.Q.	115	60–127	94.7
Performance scale I.Q.	98	62–134	95.1
Full scale I.Q.	98	61–133	97.8

TABLE 2. *Comparison of MMPI Scores Obtained at the Beginning and End of the Treatment Period*

MMPI categories	Initial mean score (N = 83)	Final mean score (N = 57)	Difference between means	SE diff.	Critical ratio
Hs	66.5	56.8	9.7	2.1	4.62
D	75.7	64.58	11.12	2.3	4.83
Hy	65.98	57.3	8.68	1.89	4.59
Pd	61.05	53.66	7.39	1.67	4.43
Mf	57.76	55.99	1.77	1.4	1.26
Pa	64.5	54.25	10.25	1.84	5.57
Pt	68.20	57.16	11.04	2.03	5.44
Sc	66.4	56.2	10.20	2.09	4.88
Ma	52.62	50.17	2.45	1.83	1.33

patients' progress, by comparing results obtained at the beginning and at the end of hospitalization. Such an approach, which disregards diagnosis, duration, severity and character of symptoms and length and type of treatment, admittedly obscures many important relationships; nevertheless, we thought that such treatment of our data, crude though it may be, would be of sufficient value to warrant the effort. The Rorschach results and the MMPI findings tend to run parallel. The Rorschach findings of improvement tend to lag. The MMPI results lend themselves better to serial study for statistical purposes than do the Rorschach results. Eighty-three MMPI scores obtained at the beginning and 57 scores obtained at the end of the treatment period served as the basis for this study. These statistics are shown in Table 2. The number of cases studied is large enough to be taken as fairly representative of the group as a whole.

In Table 2 the final mean scores are lower in all categories than the initial mean scores. The gains in all cases, except for the Mf (interest) and Ma (hypomania) scores, have critical ratios well above the point (3.00) which is generally accepted as being significant. These findings testify to the effectiveness of therapy and provide evidence of the validity of our figures, in that there is no reason for assuming that the therapy used should bring about any particular changes in those areas of personality that are measured by the Mf and Ma scales. A rationale for the modification of symptoms in the other seven areas (Table 2) by treatment can be provided, but the occurrence of sizable gains on the Mf and Ma scales would have been hard to account for. Our initial impulse was to omit any consideration of Mf and Ma scores, but we decided to include these figures as an indirect test of validity, and the results would appear to confirm the soundness of our statistical approach.

The relative magnitude of the gains on the different scales is in approximately the order that would normally be expected in a group of this type. The greatest improvement is shown on the depression scale, probably because these symptoms are common in geriatric patients and also because the results of overall therapy in the D group seem to be better than those in the mixed D and Sc group or the pure Sc group. The first observation tends to be confirmed by the fact that the initial mean score on the depression scale is the highest of the nine listed. The second highest gain is on the psychasthenia scale, a finding which probably is

to be accounted for largely by the fact that there is a high correlation between the D and Pt scales. The Pt scale seems to be a secondary D scale, and the same factors that account for improvement on the D scale probably account for the change in Pt symptoms. We were not prepared for the finding that gains on the Pa scale were third in order of size, and this is to be regarded as a rather significant outcome of our research. It is true that the initial mean score on this scale was not especially high, and that this scale is generally regarded as one of the weak factors of the test, but this finding would appear to be worthy of further investigation. As a rule we did not consider stopping electroshock therapy or insulin shock until the scores were 75 or lower. Usually the degree of insight did not permit starting psychotherapy until the scores were 70 or lower. The clinical data usually paralleled the psychologic test results. At times confusion caused bizarre psychologic findings, indicating that the patient was worse, although he was actually showing clinical improvement. Infrequently the psychologic findings were normal, although clinically the patient was very ill. The Rorschach test is most likely to lead to the latter error, and to uncover subclinical or persisting personality or emotional faults.

SUMMARY

Seven hundred psychologic tests were made on 141 geriatric patients in whom the previous diagnosis had been senile dementia. Results of the tests were used as guides to prognosis and treatment.

In the true senile dementias, the psychologic findings showed a low I.Q., marked deterioration and confusion. In the other patients the I.Q. was normal and the deterioration was usually negligible. The MMPI and Rorschach findings were divided into depression and schizoid trends and treatment was advised according to whether these trends were pure or mbined.

There were 41 patients in the organic group, and in them the influence of coexisting organic changes or concurrent illness was studied. In those with a pure depression trend, the prognosis should have been good, but it turned out to be only fair; in those with combined depression and schizoid trends the prognosis was fair; and in those with a pure schizoid trend the prognosis was poor.

There were 100 patients in the functional group. In those with a pure depression trend the prognosis was good; in those with combined depression and schizoid trends the prognosis was fair; and in those with depression and schizoid trends plus a psychopathic-deviate trend, as well as in those with a pure schizoid trend, the prognosis was poor. The exception was in patients with a pure depression trend complicated by real and persisting life problems, in whom the results were less than fair.

The occupational recovery of 85 of 141 patients in this study warrants continuation of this type of research.

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RESPIRATORY ALLERGIES AND THEIR MODIFICATIONS IN PATIENTS OVER 45 YEARS OF AGE*

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By and large, respiratory allergies in patients over 45 years of age present increasing problems of complications and differential diagnosis. Upper respiratory tract allergies and chronic infections are frequently accompanied by the development of manifestations of hypersensitiveness in the lower respiratory tract, such as allergic bronchitis, bronchial asthma, and emphysema. These pulmonary changes, if neglected or poorly managed, frequently predispose with age toward the development of permanent and irreversible pathologic structural changes. In older asthmatics, very frequently asthma is a progression from chronic sinusitis based upon an acute infection or a developing allergy earlier in life, often in childhood. Pertussis, croup, scarlatina, rubella, or other acute childhood infections, bronchopneumonia, recurrent attacks of acute tracheobronchitis, and adenitis of the upper respiratory tract may start the vicious cycle.

Regardless of the primary etiologic factor, as life goes on there develops progressive bronchial spastic disease, due either to chronic bronchial asthma or to chronic pulmonary emphysema. The pathologists have furnished evidence that these are linked together.

Allergy must now be considered as a clinical entity with its various phases integrated by known factors or implications. Therefore, this presentation aims to avoid controversial and confusing problems and deals with the practical clinical aspects of chronic respiratory allergic manifestations.

BRONCHIAL ASTHMA

This is the most important of the respiratory allergies, because of its frequency, the crippling development of complications in the older age groups, and the comparatively high death rate. In prolonged bronchial asthma, pulmonary emphysema is an inevitable complication which results in greater permanent disability than do the paroxysms of asthma. In asthmatics who have had symptoms continuously for more than ten years, chronic emphysema develops. Obviously, if the acute paroxysms can be prevented at the time of onset, the emphysema can be prevented. Patients who are taught the self-administration of epinephrine at the onset of their frequent paroxysms and who carry this out through the years, are able to prevent the development of emphysema.

It is particularly in the older age group that the instances of so-called "intrinsic" asthma occur, although intrinsic asthma in early life is not unusual.

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This term "intrinsic asthma" is commonly used when the basis of the allergic symptoms is found in the body's own proteins. In this endogenous allergy the patients are hypersensitive to allergens originating in their own bodies, such as bacteria, viruses, fungi, or certain parasites and their products. These autoallergens may be the result of autolytic influences, or degenerative or physiochemical processes. According to Scheele, formerly Surgeon-General of the United States Public Health Service, "chronic degenerative diseases occur four times as frequently among the older age groups as in the general population." Respiratory conditions, mainly bronchitis, cause about 40 per cent of the infirmities of older people.

Focal infections are a very important source of bacterial sensitization. These foci can cause and/or maintain a state of hypersensitiveness. Eventually, progressive bronchospastic disease develops, due either to chronic bronchial asthma or chronic pulmonary emphysema.

Clinical evidence of endocrine deficiencies, particularly of the sex hormones, has been noted at times to accompany an increase of allergy. In some women the first symptoms of hypersensitiveness appear during the menopause. This has been attributed to added stress, particularly in those with constitutional inferiorities.

Treatment

Treatment may be specific or nonspecific. Specific treatment consists of elimination measures and hyposensitization. If properly carried out before chronicity develops, such procedures are quite satisfactory. In the intrinsic type of asthma and also when the allergen or allergens cannot be determined or excluded, the treatment is directed toward the paroxysm itself. During acute conditions the patient is treated first and the disease later.

Epinephrine is still the agent most dramatically effective in the prompt relief of an attack. Prolonged use of epinephrine in proper physiologic doses does not have complicating effects. The more prompt its administration, the less likelihood of resulting emphysema, which is more harmful than the drug itself. An aerosol of 1:100 dilution may also be used. Ephedrine and its several compounds are less effective in adults, unless wheezing is mild. An oral dose of 75 mg. at bedtime, with an equal amount of Amytal®, may either prevent an attack or abort one already begun.

Aminophylline is very effective in relieving asthma. It is a diuretic, antispasmodic, and cardiovascular agent. It is also a powerful bronchodilator and thus allows the tenacious mucus to be easily expelled on coughing. Oral doses larger than 0.2 Gm. three times a day may produce gastric irritation. In acute conditions it is better given slowly in doses of 0.25–0.5 Gm. When hydration is necessary, aminophylline is given intravenously preferably in 500 ml. of 5 per cent glucose or one of the repair solutions, which takes into consideration that there is a fluid and electrolyte imbalance. This occurs particularly in those who are taking cortisone. There is also evidence of some serum potassium depletion and an increased level of serum sodium.

Harsh and Donovan (1) observed the effect of the wide variation of sodium and potassium intake in children with asthma. They demonstrated that a high sodium intake increased the amount of asthma, whereas high potassium intake had little or no effect. When possible, the concentration of serum sodium should be determined. If normal or slightly above, distilled water, not physiologic saline, should be used in the infusion. When there is also a low blood potassium level, basic repair solutions fluids should be used, such as Butler's, Darrow's or Baxter's electrolyte solutions. Aminophylline may be added.

At night enteric-coated tablets containing theophylline sodium acetate, ephedrine sulfate, and phenobarbital sodium (Luasmin®) give the patient considerable comfort. Similar tablets, Nephenalin® or Dainite®, have the same primary ingredients, and these plain tablets may be taken simultaneously with the enteric prolonged-action tablets at night. Sus-Phrine®, a 1:200 aqueous suspension of epinephrine in a base of 10 per cent glycerine, 2 per cent sodium thioglycolate, and 0.5 per cent chlorobutanol, may be given subcutaneously. The adult dose is 0.40 ml.

If aminophylline produces gastric irritation, Aminodrox®, which also contains aluminum hydroxide gel, increases tolerance. Oral tablets of choline theophyllinate (Choledyl), a new xanthine medication, are often effective when oral aminophylline has failed or is not tolerated. Aminophylline may be administered very effectively by rectal suppositories, each containing aminophylline 0.5 Gm., ephedrine hydrochloride 0.05 Gm., and Amytal 0.1 Gm. in a suitable base.

One of the most useful drugs in the treatment of bronchial asthma is potassium iodide, because of its direct action on the plugs of mucus in the bronchial tubes. It is most effective when given in generous doses, such as 0.5 Gm. every three hours for a few days. Quadrinal® tablets contain ephedrine hydrochloride, phenobarbital, theophylline-calcium salicylate and also 5 grains of potassium iodide—a useful combination.

ACTH and cortisone have striking effects if given in sufficient amounts. The results are dramatic when these drugs are given during an attack of intractable asthma. ACTH is administered in doses of 10 mg. per 1,000 ml. of 5 per cent glucose or water by slow intravenous drip over a period of four hours. This may be repeated if necessary. ACTH may also be given in a gel intramuscularly (40 Gm. twice a day). A corticotropin preparation (Corticotropin-Z), in which zinc salt is incorporated, has been effectively used in England (2) in giving prolonged relief, and is now under clinical investigation in this country. Each milliliter of this product contains 40 to 60 clinical units of purified corticotropin with zinc hydroxide. Zinc corticotropin injections last from twenty-four to seventy-two hours.

Oral cortisone in severe cases may have to be administered in amounts of 200 to 400 mg. per day for the first two days, with diminished amounts thereafter. This method of treatment of status asthmaticus has taken the place of all others. In the milder forms of bronchial asthma, cortisone is given in doses of 50 to 100 mg. a day over a period of months, and has given great relief in chronic situations. It has been useful in the nonatopic type and lessens the severity of the

asthma to a greater degree than the former conventionally-used medications. This treatment demands certain precautions, however, particularly a low-sodium intake.

Indiscriminate use of oxygen may reverse pulmonary ventilation, due to carbon dioxide narcosis. Oxygen inhalation should be given under positive pressure at short intervals, since the force of inspiration alone is not sufficient for proper ventilation. For emergency relief only, Demerol® is permissible, but never morphine. Deeper sedation may be satisfactorily obtained by rectal instillation of paraldehyde in a dose of 15 ml. mixed well with 60 ml. of olive oil. The dose may be repeated if necessary.

When infection complicates bronchial asthma, a serious problem arises. Pus in the bronchi adds to the irritation, and is the main reason for the intractability of many cases. Treatment is similar to that of bronchitis. Sputum cultures should be made if possible before giving any of the chemotherapeutic agents, such as penicillin. If this is not feasible, it should be determined whether or not the patient has received any antibiotic in the past without side effects. If so, this one should be tried first. All the antibiotics should be tried in large doses in infectious asthma. Any one of the broad-spectrum type which has given good results should be continued. Following such a course, asthma is frequently greatly relieved and will more readily respond to iodides, ephedrine, and other medication. Aerosol antibiotics have been unsatisfactory.

The patient with chronic bronchial infection complicating asthma will get along much better where there is warm even weather throughout the year. This applies also to asthmatics whose condition is not complicated by infection, because they avoid cold air, fog, smoke, and occasional specific allergens in their environment. Some use bacterial vaccines selected on the basis of skin reactions; it is thought that temporary benefit may be due to stimulation of the adrenals.

In a study of fatal cases of bronchial asthma, it was found that most of the patients suffered from gross emphysema, bronchial plugging, hypertrophy of the bronchial walls with eosinophilic infiltration, and overactivity of the mucous glands of the bronchi. In about half of 160 cases studied, asthma was the only, or chief cause of death; in the other half the secondary causes of death included bronchopneumonia, right ventricular hypertrophy, persistent thymus, and pneumothorax. More than half of the patients were between 40 and 60 years of age (3).

EMPHYSEMA

Emphysema, the inevitable complication of asthma, offers another serious problem. Tenney (4) has shown that in patients with emphysema, when oxygen mixtures containing 3.3 and 4.7 per cent carbon dioxide are used for fifteen minutes, the inspired carbon dioxide is less effective in increasing ventilation than in normal individuals. Reduction of the blood bicarbonate content by means of Diamox® (24 mg./Kg. body weight) increases the ventilatory response of the emphysematous patient to inspired carbon dioxide. The higher the plasma bicarbonate level, the lower the ventilatory response to carbon dioxide, which is an indication for a low-sodium intake in cases of pulmonary emphysema.

Simpson (5), in studying 118 patients suffering from emphysema complicated by acute respiratory infection, observed that 41 died in the hospital and 34 more died within twenty-one months after discharge. The 41 patients dying in the hospital showed severe bronchiolitis, emphysema, and right ventricular hypertrophy. Coma and cerebral symptoms may follow the administration of oxygen. After-care in these cases must include the use of antispasmodics and breathing exercises.

Geschickter and Popovici (6) in a study of 75 asthmatic patients more than 40 years of age noted that 60 suffered from emphysema and that 28 of these emphysematous patients had a blood pressure greater than 160/90 mm. Hg. This was almost double the expected incidence of 20 to 25 per cent. It was suggested that emphysema causes hypertension because of increased intrapleural pressure, leading to a higher venous pressure and therefore to venous congestion of the kidneys and a reflex compensatory arteriolar spasm. Of the 60 patients with asthma and emphysema, 21 showed electrocardiographic evidence of myocardial damage, which the authors believed to be caused by raised intrathoracic pressure interfering with the coronary venous return to the right auricle. The myocardial damage was considered to be a result of coronary venous congestion.

Barach (7) breathing exercises are very helpful for patients with pulmonary emphysema. The Gordon-Barach abdominal support (Spencer Company) has been found to be the most effective type in the treatment of emphysema. It contains two spring metal bands that not only support the lower abdomen and increase the intra-abdominal pressure, but also store mechanical energy during the inspiratory phase of respiration, which is then employed during the expiratory cycle through recoil of the two spring bands. The combination of diaphragmatic breathing and the Gordon-Barach support may bring about a substantial relief from shortness of breath on exertion. Thus in patients with pulmonary emphysema the elastic recoil of the lung is assisted by mechanical aids to breathing.

Cardiac complications of asthma develop in advanced emphysema, and cor pulmonale may occur. The signs of emphysema and cardiac failure may be similar, in that there is a large amount of dependent edema, due to increased capillary pressure and anoxemia. At autopsy there may be no demonstrable cardiac lesion. Dyspnea on exertion, reduced vital capacity, cyanosis, increased venous pressure, a liver displaced downward by a low diaphragm, basal rales from bronchitis, and distant heart sounds may occur in both emphysema and cardiac insufficiency. Shortness of breath, cough, and pulmonary signs of bronchospasm resulting from true allergic bronchial asthma are not relieved by an injection of Mercuhydrin®, whereas cardiac asthma responds well. This serves as a useful guide in differentiating between cardiac and bronchial asthma (8).

The most common causes of primary chronic cor pulmonale are emphysema, asthma, and bronchiectasis, which frequently appear in combination. Any chronic infection which may cause pulmonary fibrosis is a factor. There usually is a history of long-standing chronic cough, and some patients have a special type of substernal pain, brought about by exertion and relieved by rest, or induced whenever there is an increase in the underlying pulmonary condition.

Medication directed toward eliminating the pulmonary condition gives more relief than the usual nitrite therapy for coronary pain. However, clinical, electrocardiographic, and radiologic evidence of right-ventricle hypertrophy are often absent. When preventing or controlling acute respiratory infections, which usually aggravate right ventricular failure, penicillin should be used in doses of 100,000 units twice daily. The acute infections are treated according to the infecting agent. Sputum cultures and sensitivity tests are indicated. Measures to be taken to facilitate ventilation include administration of isopropyl norepinephrine (Isuprel®), 15 mg. sublingually two to four times a day.

In emphysema, as in bronchial asthma, aerosol therapy with a solution containing epinephrine and glycerine, as well as the use of aminophylline in full dosage three times a day, and expectorants such as potassium iodide, are valuable. Here again, oxygen should be used cautiously and intermittently, as long-continued use may cause carbon dioxide narcosis. Carbon dioxide narcosis may be precipitated suddenly by rapid relief of anoxia, but usually the narcosis develops insidiously when oxygen is used continuously. Digitalis, if used in conjunction with other procedures, may give striking benefit.

Periarteritis nodosa is a rare complication of chronic bronchial asthma, and is usually associated with the "intrinsic" type. There is an increased eosinophilia only in the presence of bronchial asthma.

BRONCHIECTASIS

The question remains controversial whether asthma can cause bronchiectasis, or whether bronchiectasis results from the same infectious process that first produces the sensitization which leads to asthma. Goodale (9) and others offer evidence that 70 to 90 per cent of their patients with bronchiectasis had some degree of sinusitis. Watson and Kibler (10) of Tucson, Arizona, found convincing evidence of allergy in the majority of their patients with bronchiectasis, most of whom had moved to Arizona from elsewhere. The sequence of pathologic changes in the development of bronchiectasis may be explained on the basis of an initial basic allergic bronchitis which eventually leads to an atelectasis; this, in turn, is followed after a variable period by bronchiectatic dilatation. Symptoms become more manifest when the dependent bronchi are involved.

Bronchography, using an opaque medium in the side position, is the most important step in the diagnosis of bronchiectasis. In cases of long-standing asthma there may be non-excreting bronchi, forming purulent accumulations in which there is no dilatation. This condition is called septic bronchitis and the hazard is graver than in bronchiectasis. The bronchogram, therefore, can include demonstration of bronchial abnormality, but cannot always exclude its possible presence. The roentgen interpretations should be correlated with other significant material. If the atelectasis is accompanied by interstitial involvement of the bronchial wall, a permanent interference with the peristaltic and ciliary functions of excretion may develop. Lack of these excretory functions in the dependent bronchi results in a reservoir that collects and concentrates secretions; these become viscid and are extremely difficult to expel until bacilli liquefy the medium.

The infected tubes act as incubators, representing a dangerous focus of infection. The only cure of septic bronchiectasis is excision. When this is contraindicated, postural drainage, abstaining from irritants, and intelligent use of antibiotics may alleviate the condition.

BRONCHOSTENOSIS

According to Prickman and Moersch (11), bronchostenosis is a relatively common complication of severe asthma. The stenosis consists of a definite stricture-like narrowing of the bronchus, which is probably primarily inflammatory and nonallergic in nature. The site is usually in the lower posterior portion of the lungs. Stenosis should be suspected if there is suppression of breath sounds and impairment of tactile fremitus. Roentgenologic findings are similar to those in atelectasis, complicated occasionally by signs of bronchiectasis. Temperatures of 101° to 103°F. are common for several days. The sputum is mucopurulent and may be blood-streaked. Treatment consists of bronchoscopy, and dilatation of the stenosed bronchus, followed by aspiration of the retained secretion. Therapy with a broad-spectrum antibiotic should be tried.

NASAL ALLERGY

Time will not permit within the scope of this paper a discussion of the etiology, diagnosis, and pathogenesis of seasonal hay fever. They are generally known. Vasomotor rhinitis or perennial allergic rhinitis, along with sinus disease, are terms frequently used to indicate concomitant manifestations of the same condition in different sites. In adults and older people inhalants are predominant as the etiologic factor, particularly house dust and its various components. The condition is frequently encountered in cases of asthma, and in almost half of these cases the nasal condition appears simultaneously with the asthma and is considered due to the same agent. The early recognition and treatment of nasal allergy, before asthma has developed, is an important element in the prophylaxis of asthma. According to Black (12), after 50 years of age not more than 5 per cent of persons in whom dyspnea develops have bronchial asthma alone.

When exclusion or avoidance measures do not influence the symptoms, infection is likely to be present. If so, a cytologic study of the nasal secretions will show many eosinophils and pus cells. The allergic symptoms persist until the infection is reduced. A group of cases may show no infection, yet strict environmental control does not relieve the symptoms, which may be very severe. Such patients, particularly in the older age groups, follow the pattern seen in so-called "intrinsic" asthma; the disease is frequently intractable to treatment. Drug therapy is the same as that for hay fever.

When the etiologic agents can be determined, avoidance and immunologic measures should be tried. For many years medication with ephedrine or one of its isomers (orally, or by nose drops) was the usual procedure. The introduction of the antihistaminic drugs was a decided advance in the treatment of nasal allergies. They are most effective when used as supplementary treatment to immunologic measures, although when used alone they may relieve symptoms in

the milder or moderately severe cases. There is no one antihistaminic drug which works equally well for all patients. Several should be tried, and one should be selected which for the particular patient, shows the fewest side reactions with the maximum beneficial effect. When tolerance to any one antihistaminic agent seems to be reached, another one should be used for several weeks. Even though it should prove to be not as effective, it will frequently pave the way for a return to the former drug. Oral administration in the form of tablets, capsules, or solutions is the usual procedure, but there are also a number of combinations of these antihistaminics with other antiallergic compounds, such as ephedrine, aminophylline, stimulants, salicylates, and cough mixtures. In an allergic emergency, hypodermic injection of an antihistaminic agent may supplement ephedrine or aminophylline. In allergic cough or moderate asthma an aerosolized form may be effective. Some are more suitable for daytime use and others for prolonged or sustained effect at night. It may be advantageous to combine two antihistaminic drugs, one short-acting and one long-acting (Dibistine®). Some are in ordinary coated tablets and others in specially coated tablets that release the drug over a longer period of time. When there is a combined upper and lower respiratory allergy, antihistamine medication may be prescribed in conjunction with ephedrine and aminophylline, provided an expectorant is also prescribed. The latter is important. Naturally, for daytime use the antihistamines with the least sedative action are preferable. At night larger doses may be given, particularly of those with a more sedative action. Long-acting antihistaminic drugs include Phenergan®, Di-Paralene®, Perazil®, Pyronil®, and chlorprophenpyridamine maleate (either as prolonged-action tablets of Chlor-Trimeton®, or as Spansules® of Teldrin®). For general use intermediate drugs are indicated, such as Chlor-Trimeton (plain or prolonged-action tablets), Pyribenzamine®, Histadyl®, Neo-Antergan®, and Pyrrolazote®. When the therapeutic dose is quite small, as with 4-mg. tablets of Chlor-Trimeton, the occurrence of side reactions is minimized.

When acute infection is superimposed upon a nasal allergy, Coricidin® (an antihistaminic-analgesic compound which contains aspirin, acetophenetidin, caffeine, and Chlor-Trimeton) for three days at the outset of the infection may give considerable relief. Before administration, sensitivity to aspirin should be determined if possible, although the presence of the antihistaminic agent lessens the chance of such sensitivity. Coricidin® is prepared also with codeine as well as with penicillin G procaine. The latter affords antibiotic protection, combats bacterial invaders, and checks extension of the infection. Use of injectible Chlor-Trimeton virtually eliminates reactions to penicillin and also to other commonly injected medications, including allergenic extracts. It is administered intramuscularly or subcutaneously.

Cortisone, given temporarily on days of severe symptoms, may be beneficial. A nasal spray which is isotonic, antiallergic, antibacterial, decongestant, and mucolytic, and which frequently gives immediate dramatic relief, is Biomydrin®. The local application of hydrocortisone (Cortone® F) to the nasal mucosa by means of drops, or in the form of a mist (such as Cortogen® Suspension or Vasocort®), often is of immediate benefit.

PSYCHOLOGIC FACTORS

When we consider respiratory allergies in the older age groups, we sometimes forget psychologic factors. It would be time-consuming to differentiate between cause and effect and be able to say in each case that psychoneuroses caused the allergic manifestations or that the latter caused the psychologic disorders. These factors probably interact; but I do know that the better I practice allergy, the fewer psychoneuroses I am forced to treat. The fact that we do not know the answer does not invalidate our observation that there is an interaction of these factors. They give rise to serious problems which frequently result in crippling diseases of the aged. It is no wonder that the interest in allergy is increasing rapidly.

There is still much need for research and teaching. The American Foundation for Allergic Diseases is now fully established with headquarters in New York. Your interest and support are earnestly sought.

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THE SURGICAL TREATMENT OF HUMAN HYPERTENSION

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Hypertensive cardiovascular disease accounts for many deaths and much premature disability in young and middle-aged persons, particularly those in the fifth and sixth decades of life. This is especially true for male individuals, who do not tolerate the disorder as well as females. Over the years many forms of treatment have been introduced to combat hypertension, but since the etiology of the most widely prevalent variety of the disease remains unknown, all of these measures have been empirical and no single method of treatment has been entirely satisfactory. The principal methods at present include 1) diets low in sodium and fat, 2) drugs with a hypotensive or sedative effect, 3) surgical operations upon the sympathetic nervous system, and 4) combinations of the foregoing three methods. Treatment by total or subtotal adrenalectomy is still in the investigative stage.

Occasionally hypertension is due to a recognizable cause and may be cured by surgical means. This small group includes hypertension due to pheochromocytoma, to adrenocortical adenoma, to unilateral renal disease, to coarctation of the aorta, and to Cushing's disease. Such patients probably comprise less than 1 per cent of the total hypertensive population but are nevertheless a very important group. Unfortunately, the largest number of patients with high blood pressure have essential or malignant hypertension, and it is with this form of the disorder that we are primarily concerned.

METHOD OF STUDY

Patients who present themselves with high blood pressure must be evaluated thoroughly, so that curable forms of the disease may be recognized and an accurate estimate be made of the cardiovascular status of patients with essential or malignant hypertension. In this way patients with severe and progressive cardiovascular disease will not be denied the benefits of maximum treatment. A detailed history and physical examination should be made and data should be recorded regarding the cerebral, cardiac and renal areas. The cardiac status is determined by an electrocardiogram and a seven-foot heart roentgenogram, with particular reference to the size and shape of the heart and the state of the

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aorta. In patients with significant degrees of tachycardia or those with angina pectoris, Master's two-step exercise test is used for further appraisal of the cardiac situation. The status of the kidneys is evaluated by urinalysis, a 12-hour concentration test, an intravenous pyelogram, and an intravenous phenolsulfonphthalein test. In the latter, the dye is injected after a period of forced fluid intake, and specimens are collected at intervals of fifteen and thirty minutes and of one and two hours. This simple test of renal function has been found very useful in estimating the extent of renal damage in hypertensive patients and is the one upon which we place the most reliance. A serum nonprotein nitrogen determination is also made.

The blood pressure responses of the patient are measured 1) under change of posture, with the added stimulation of cold, and 2) under sedation. The posture-cold test is performed as follows: Ambulatory readings are taken as soon as possible after admission to the hospital. After at least forty-eight hours of bed rest, except for lavatory privileges, the resting values are recorded. The test can also be carried out routinely on an ambulatory basis in the office, preferably by a technician rather than the physician, since the physician often acts as a pressor stimulus to the patient. Preliminary readings of blood pressure are taken on each arm. If no great discrepancy exists, the right arm is used. If there is a marked difference between the two sides, repeated checks are made, and the arm with the higher reading is selected. The test is explained to the patient and after an additional rest period of fifteen to twenty minutes in the horizontal position, observations are begun. It is essential that the environment be quiet and comfortable.

Pulse and blood pressure readings are taken every minute for five minutes with the patient first lying and then standing. With the patient again horizontal, three more blood pressure readings are taken at two-minute intervals. Then the opposite hand is immersed up to the wrist in ice water at 4° to 5° C. for exactly one minute. Blood pressure readings are taken after thirty seconds and at the end of sixty seconds of stimulation by cold. Readings are continued at two-minute intervals for an additional three readings. The patient then assumes the upright position and after three preliminary readings at two-minute intervals, the cold stimulus is repeated exactly as in the horizontal position. This is followed by three additional readings at two-minute intervals. The average of the first five readings in the horizontal position during the first portion of the posture-cold blood pressure test is regarded as the *resting blood-pressure level*. The diastolic readings are considered the more important.

The sedative test is performed in all patients who are hospitalized. Following a light supper, 3 grains of sodium amytal are given by mouth at 7:00, 8:00 and 9:00 p.m. Hourly readings of pulse and blood pressure are recorded from 7:00 p.m. to 7:00 a.m. The lowest reading of systolic and diastolic blood pressure is taken as the response. This is evaluated by comparison with the average horizontal resting blood-pressure level as determined by the posture-cold test, the diastolic response being the more significant. To be regarded as satisfactory, the diastolic level during the sedative test should fall to 90 mm. or less in pa-

tients with resting diastolic levels between 100 and 119 mm. of mercury. In patients with resting diastolic levels between 120 and 139, the sedation response should be a fall to 100 mm. or less. In those with resting diastolic levels of 140 mm. or more, the diastolic level should fall to 110 mm. or less. Otherwise, the response to sedation is regarded as unsatisfactory.

Following the complete work-up, the patients are classified into groups. It has been pointed out many times that the prognosis for a hypertensive patient varies according to the status of his cardiovascular system when first examined (1). Unless patients with similar degrees of hypertension and of cardiovascular involvement are placed in comparable groups, there is no basis for the comparison of results of treatment. A study of the literature reveals that the mortality rates for different groups of patients who have not been operated on varies tremendously—from 17 to 91 per cent (2). This is largely a matter of classification of patients. Since there are many factors which influence prognosis, we have attempted to control as many as possible by adopting the plan described here, which we have used for many years. This system makes the clinical material in each group as comparable as possible and is the best that we have been able to devise with the number of patients we have studied. The various factors which have a bearing on prognosis are listed in Table 1, a numerical value being assigned to each. In any given patient the existing factors are totaled, resulting in the *numerical grade* for the patient (Table 2). The patients are then placed in four groups. If the numerical grade is less than 4, the patient is in Group 1 or 2. If the numerical grade is 4 or more, the patient is in Group 3 or 4. The additional factors that determine the exact group of the patient are given in Table 3. Patients in Group 1 have the least severe cardiovascular disease, whereas those in Group 4 have the most severe degree of cardiovascular damage.

TABLE 1. *Numerical Values of Various Factors which Influence Prognosis*

	Numerical value of each factor
Age 50 or over	1
Cerebrovascular accident, with or without minor residual	
Abnormal ECG	
Enlarged heart	
Impending congestive failure	
Mild angina	
P.S.P.* less than 25% in 15 min., or less than 60% in 2 hrs	
Cerebrovascular accident, with residual†	2
Frank congestive failure, moderate angina	
P.S.P.* less than 20% in 15 min	
Unsatisfactory response to sedation	
P.S.P.* less than 15% in 15 min	3
Nitrogen retention	4

* Phenolsulfonphthalein concentration in urine.

† Cerebral deterioration or definite involvement of arm and/or leg.

TABLE 2. *Two Examples of Method for Determining Numerical Grade of Hypertensive Patients*

Factors considered	Numerical value
Example 1	
Abnormal ECG	1
Cerebrovascular accident without residual	1
P.S.P.*—20% in 15 min	1
(Total)	3—Numerical grade
Example 2	
Abnormal ECG	1
Enlarged heart	1
P.S.P.*—10% in 15 min	3
(Total)	5—Numerical grade

* Phenolsulfonphthalein concentration in urine.

TABLE 3. *Classification of Hypertensive Patients*

Criteria for Grouping

Group	Numerical grade	Other factors
1	Less than 4	Eyegrounds, grade 0 or 1. No changes in cerebral, cardiac or renal areas.
2	Less than 4	Eyegrounds, grade 0 or 1, with changes in cerebral, cardiac and/or renal areas. Eyegrounds grade 2, 3 or 4, with or without changes in cerebral, cardiac or renal areas.
3	4 or more	Resting diastolic level of B.P. below 140 mm. Changes in cerebral, cardiac and/or renal areas do not include the following: (a) C.V.A. with marked residual. (b) Frank congestive failure. (c) P.S.P. below 15% in 15 min., associated with a poor response to sedation.
4	4 or more	Resting diastolic level of B.P. below 140 mm., combined with one or more of the following: (a) C.V.A. with marked residual. (b) Frank congestive failure. (c) P.S.P. below 15% in 15 min., combined with a poor response to sedation. Resting diastolic level of B.P. of 140 mm. or more.

It should be pointed out that the patients under discussion all had *persistent hypertension*, not the intermittent variety. The blood pressure in the resting horizontal position after two days of bed rest in the hospital was 140/90 mm. of mercury or more. These patients had advanced through the earlier stages of the natural history of hypertension, *i.e.*, hyper-reactivity of the blood pressure without hypertension, and intermittent hypertension brought on by various stimuli, and therefore represented unusually severe forms of the disorder. They did not fall into that group of patients with hypertension who tolerate it well and may have long useful lives without any treatment. The great majority (88 per cent)

of our patients, when first seen, had manifest vascular disease either in the eyes, heart, kidney or brain and were therefore in the stage of hypertension when cardiovascular complications had begun to occur.

SPLANCHNICECTOMY FOR ESSENTIAL HYPERTENSION

The surgical maneuver which has been employed most commonly in the treatment of essential or malignant hypertension is thoracolumbar splanchnicectomy. This operation was used in 93 per cent of our surgically treated patients. The sympathetic trunks were removed bilaterally from D8 to L1 inclusive together with the greater, lesser, and least splanchnic nerves. The adrenal glands and kidneys were carefully explored at the time of operation, which is almost always a one-stage procedure. An additional 7 per cent of surgically treated hypertensive patients underwent transthoracic sympathectomy and splanchnicectomy. These were patients who had 1) coronary artery disease and/or angina pectoris associated with hypertension, and 2) exertional, emotional, or postural tachycardia associated with hypertension. The sympathetic trunks were removed bilaterally from C3 to D12, inclusive, together with the greater and lesser splanchnic nerves in the patients with angina pectoris. For the patients with unusual tachycardia and hypertension without angina, the sympathetic trunks were removed from D2 to D12, inclusive, together with the splanchnic nerves. This report is concerned with the effect of thoracolumbar splanchnicectomy upon the course of hypertensive cardiovascular disease.

Since thoracolumbar splanchnicectomy was first introduced in 1938 we have studied more than 3,500 hypertensive patients. Over 2,400 of these have been operated upon and the rest have been treated medically. A continuous follow-up program is in operation. Since the data in the literature were not entirely satisfactory as control material for our surgical series, we used the medical patients that we have studied and followed for at least five years and at most, fifteen years. Patients within the surgical and medical groups have been studied and classified in exactly the same fashion. To date, 1,266 patients have been operated upon and followed five years or more (representing a 90 per cent follow-up), and 467 medical control patients have been studied and followed five years or more (representing an 88 per cent follow-up). The average age of the surgical patients was 42 years and that of the medical patients was 45 years. About 70 per cent of the patients were 40 years of age or older and about 25 per cent were over the age of 50. We have tended to be more conservative in offering surgical treatment to patients over the age of 50, but in recent years more elderly patients have been operated on than in the early years of the study. Patients over 50, or even those over 60, may be benefited greatly by surgical treatment. The operative mortality following splanchnicectomy has been 0.7 per cent in Group 1, 1.4 per cent in Group 2, 4.3 per cent in Group 3, and 10.9 per cent in Group 4, with an overall operative mortality of 2.8 per cent.

Table 4 lists the mortality rates for nonsurgically and surgically treated hypertensive patients who have been followed for five years or more after operation or after study. The statistical analysis of these five-year results is also

TABLE 4. *Mortality Rates for Nonsurgically and Surgically Treated Hypertensive Patients Grouped According to Smithwick Criteria*

Group	Nonsurgical series		Surgical series	
	No. of cases	Mortality at 5 years	No. of cases	Mortality at 5 years
		%		%
1	62	19	158	8
2	200	38	735	13
3	108	71	244	20
4	97	90	129	59
Totals.....	467	54	1,266	19

Statistical analysis* of the comparative 5-year mortality rates between the nonsurgical and surgical groups is as follows:

Group	Chi-square	p	Significance
1	4.92	0.03	Significant
2	60.6	0.001	Highly significant
3	83.2	0.001	Highly significant
4	24.6	0.001	Highly significant

Yates correction used throughout.

* Analysis made by Mr. John Alman of Boston University.

5732 p. 1

listed. Figure 1 illustrates the survival curves for the same patients. These survival curves have been constructed, using the actuarial method as described by Berkson and Gage (4).

A study of the data reveals that the mortality rates in all four surgical groups are significantly lower than those for the corresponding medical groups. This is particularly true for Groups 2 and 3, in which the differences are striking and highly significant. The difference is also significant in Group 1 and, although the difference in Group 4 is highly significant, this group carries a poor prognosis even with surgical treatment. These differences are illustrated in a striking fashion by the survival curves in Figure 1, in which a curve of the survival rate of the normal population of the same age is also plotted for comparison.

The survival curves also indicate the severity of the hypertensive disease of the patients under consideration. It should be emphasized that patients with persistent hypertension and evidence of cardiovascular damage should receive the benefit of maximum treatment, since their outlook becomes progressively poorer if they are allowed to deteriorate untreated. If surgical treatment is to be employed, it is best utilized before the disease progresses to the Group 4 stage.

The important factor to be considered in the evaluation of any form of treatment for hypertension is its influence on the mortality and survival rates. One may argue over blood pressure determinations, or whether cardiovascular disease is improved or not, but if the patient has expired the argument ceases. In the final analysis, the most important criterion of any form of treatment is

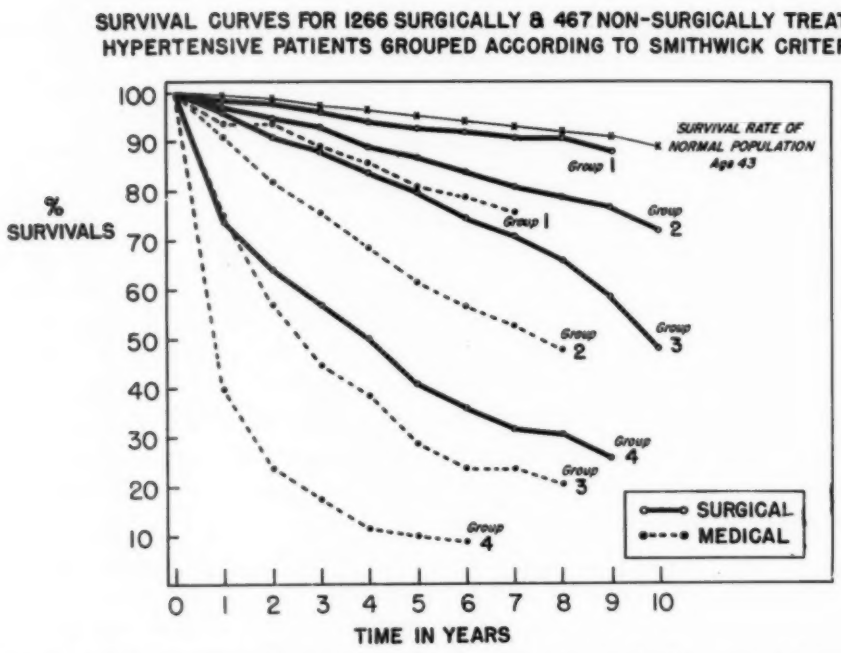

FIG. 1. Survival curves for 1,266 surgically and 467 medically treated hypertensive patients. These curves were constructed, using the actuarial method. All patients were followed for at least five years and some for as long as fourteen years, but the curves were not carried beyond the 10-year mark in any case, because either the number of cases was too small to be significant or no further deaths occurred. (Reproduced by permission, from Smithwick, R. H., and Thompson, J. E.: Splanchnicectomy for essential hypertension, *J.A.M.A.* **152:** 1501–1504 (Aug. 15) 1953.)

whether or not the patient lives longer and feels well during such a period of time.

The effect of splanchnicectomy on the level of blood pressure is of considerable interest. Our data show that about 50 per cent of patients who have had the operation show a significant lowering of blood pressure in the subsequent five-year period. In the second five years about 45 per cent show a significant lowering of blood pressure. Therefore, if the blood pressure comes down in the early years after splanchnicectomy it will remain at a favorable level in the later years following operation. It has been demonstrated to our satisfaction that lowering of blood pressure in hypertensive patients is not harmful, provided such lowering is not excessive. This is the case with surgical treatment. The prognosis for patients whose blood pressure is lowered after splanchnicectomy is significantly better than for those whose blood pressure is not lowered by operation (5). In fact, if the blood pressure can be lowered, the five-year mortality rates for patients in Groups 1, 2, and 3 approach that of the normal population. The mortality rate for Group 4 patients can also be greatly decreased. If the blood pressure can be reduced by surgical (physiologic) means, it appears that the outlook will be improved.

Another very important observation, however, is that the outlook for hypertensive patients, both as regards life expectancy and progress of cardiovascular

disease, can be improved by splanchnicectomy *even if the basal blood pressure levels are not significantly lowered postoperatively.* This is true for patients in Groups 2 and 3 especially, and for some patients in Group 4. We have in our file many examples of patients who, when checked many years after operation, show significant degrees of improvement in cardiovascular disease in all areas of the body but whose blood pressures appear to be at the same levels as they were preoperatively (6). One of the possible explanations for this improvement is the fact that certain reflex vasoconstrictor blood pressure responses are abolished after splanchnicectomy (5). It should also be pointed out that the preoperative blood pressure readings are horizontal diastolic levels obtained after the patient has rested for two days in the hospital, whereas the postoperative readings are nearly all taken on an ambulatory basis after the patient has rested only half an hour. It is highly probable that if it were feasible to obtain postoperative readings after forty-eight hours of bed rest, many more patients would be found to have significantly lowered blood pressure levels.

SELECTION OF THERAPY FOR PATIENTS WITH ESSENTIAL OR MALIGNANT HYPERTENSION

On the basis of our mortality and survival rates, certain specific recommendations can be made regarding selection of therapy for patients who present themselves with persistent hypertension and with varying degrees of cardiovascular disease. For Group 1 patients, the usual treatment consists of diet and drugs. In this group the data as yet do not allow us to make routine recommendation of surgical therapy, but it should be employed in the male patients, since it is well known that males do not tolerate the disease as well as females and since our data indicate a highly significant difference between the results of medical and surgical treatment. Surgical measures may be employed for young patients with resting diastolic blood pressure levels above 110, for those with intractable symptoms, for females with a history of toxemia or other complications of pregnancy associated with hypertension who desire more children, and for patients who will not or cannot follow a medical regimen.

Splanchnicectomy is our first choice of treatment for patients in Groups 2 and 3. In Group 2 and 3 patients who are refractory, diet and drugs may be added to the regimen. Operation may be recommended in Group 4 cases, provided renal function is adequate. The two positive contraindications to splanchnicectomy are severe kidney damage, as indicated by persistent evidence of nitrogen retention, and cerebral vascular accidents resulting in extensive paralysis or cerebral deterioration. Medical therapy in the form of diet and certain drugs is indicated for those patients of Group 4 who should not undergo operation. Although the mortality rate after operation has improved, the eventual mortality rate for Group 4 cases is still high. The combination of surgical treatment, diet and carefully selected drugs, gives the best results in the most refractory cases. It seems that less drastic diets are required after operation, since these patients appear to be more sensitive to sodium restriction. Also, postoperative patients are much more responsive to hypotensive drug therapy. The division of our patients into groups, on the basis of the follow-up survival statistics, seems at

the present time to be the only reliable basis for the selection of patients for splanchnicectomy. We are awaiting with interest the results of the long-term study of patients who have been treated by means of the more recently introduced hypotensive drugs. It will be a good many years, however, before a final evaluation of such drug therapy can be made. At this time we can only suspect that the late results will not compare favorably with those of combined medical and surgical therapy.

ADRENAL GLAND SURGERY FOR HYPERTENSION

Pheochromocytoma

Pheochromocytomas are tumors of the adrenal medulla and represent a curable form of hypertensive disease. The incidence in our series was about 0.5 per cent. Although these tumors are most commonly found in the adrenal medulla, they also occur in other locations outside the adrenal gland. They cause paroxysmal or persistent hypertension, which at times may be almost indistinguishable from essential hypertension. It is distressing to note in the literature that only at autopsy has the diagnosis of pheochromocytoma been made in about 66 per cent of reported cases (7). One must have a high index of suspicion to establish the diagnosis. There are certain signs and symptoms which are characteristic of the tumor. They are excessive sweating, peripheral vasomotor phenomena, elevated body temperature, a normal cold-pressor blood pressure response, a fasting blood sugar level of 120 mg. per 100 ml. or more, a basal metabolic rate of +20 per cent or higher, postural tachycardia, postural hypotension, paroxysmal attacks and glycosuria. An intravenous pyelogram may be very helpful or even diagnostic. The use of certain drugs has improved the percentage of correct diagnoses. The most recent such drug is Regitine. Our series consists of 16 patients with pheochromocytoma. One patient was moribund upon admission and was not operated upon. There was 1 operative death, in an elderly patient with a recent subarachnoid hemorrhage. Of the remaining 14 patients, 13 experienced lowering of the blood pressure to normal levels, and 1 had a significant reduction, though not quite to normal. One of the tumors was located in an extra-adrenal position, among the great vessels in the upper abdomen.

Adrenocortical adenoma

Yellow adenomas of the adrenal cortex, of varying size, were found in about 5 per cent of our hypertensive patients undergoing splanchnicectomy. They were routinely removed but never appeared to be the cause of the hypertensive state. In only 1 patient did the blood pressure return to normal following simple excision of an adrenocortical adenoma. This tumor, however, was of a different variety.

Cushing's disease

Most patients with Cushing's disease have an associated hypertension which may be markedly improved following subtotal or total adrenalectomy. In most cases the adrenal glands are hyperplastic. Operation usually consists of complete removal of one adrenal and of all but 2 grams of the other adrenal.

Total and subtotal adrenalectomy

The recent advent of adequate adrenocortical replacement therapy has made possible the operation of total and subtotal adrenalectomy for the treatment of essential and malignant hypertension (8). This procedure is still in the investigative stage, since it has not been shown that either subtotal or total adrenalectomy, alone or in combination with various forms of sympathectomy, has more to offer than does thoracolumbar splanchnicectomy alone. Occasional patients have been benefited by adrenalectomy who had not been helped by all the other available forms of treatment, but whether or not the overall outlook is sufficiently hopeful to justify its widespread use remains to be seen. It would appear that its usefulness is highly limited at best, and the procedure must be regarded as experimental at present. It is to be hoped that some method of identifying the occasional case which will benefit by adrenalectomy will be discovered, so that the widespread production of Addison's disease can be avoided.

UNILATERAL RENAL DISEASE

The renal origin of essential hypertension has not yet been established, in spite of much work on the subject. There are occasional cases of hypertension in man, however, which can definitely be attributed to unilateral renal disease. Such disease may be either parenchymal or vascular in origin. Most of these patients have pyelonephritis. Nephrectomy for unilateral renal disease in hypertension may effect a marked improvement in blood pressure levels and cardiovascular disease. Twenty-four per cent of nephrectomies for hypertension reported in the literature have been successful in this regard (9). In general, the indications for nephrectomy in hypertensive patients are essentially the same as in nonhypertensive patients. It appears that patients who have renal-artery lesions are much more likely to obtain a worthwhile result from unilateral nephrectomy than are those who have parenchymal disease such as pyelonephritis. The number of patients with renal-artery disease, however, is small compared to the number with parenchymal lesions. Only seriously affected or nonfunctioning kidneys should be removed. It is inadvisable to remove the poorer of two involved kidneys.

All patients with hypertension should have thorough renal study. The increased use of aortography may bring to light additional cases of hypertension due to renal-artery disease. There is a characteristic clinical picture in certain patients with hypertension caused by unilateral renal disease which, if recognized and treated promptly, may result in complete cure: 1) a short history of hypertension, 2) a rapidly progressive and downhill course, 3) severe headaches and retinopathy, and 4) a diastolic blood pressure of 130 mm. of mercury or more. In such instances, a dramatic result may be obtained by unilateral nephrectomy, if instituted early when the function of the uninvolved kidney is normal or nearly so.

In our entire series of hypertensive patients, there were only 2 cases in which the hypertension was undoubtedly due to unilateral renal disease and was relieved by nephrectomy. One patient had thrombosis of an aneurysm of the right

renal artery and the other had an arteriosclerotic occlusion of the left renal artery. In both patients, blood pressure was restored to normal and there was a complete reversal of cardiovascular disease. It is of interest that in many of our patients with essential hypertension and severe degrees of nephrosclerosis (on the basis of renal biopsy studies) both the blood pressure and the cardiovascular disease have been reversed by means of splanchnicectomy.

SUMMARY

1. A method of study and classification of hypertensive patients has been outlined.

2. Current surgical measures which are available for the treatment of hypertension have been listed.

3. The effects of splanchnicectomy upon the course of hypertensive cardiovascular disease have been presented in detail.

4. Splanchnicectomy is the treatment of first choice for males and certain females in Group 1 (least severe cardiovascular disease).

5. Splanchnicectomy is the treatment of first choice for males and females in Groups 2 and 3.

6. Splanchnicectomy is justifiable in males and females of Group 4 (most severe cardiovascular disease) provided renal function is still adequate and cerebral damage is not too extensive. The late results are poor at best in most Group 4 cases, in spite of surgical procedures, either alone or combined with the best medical treatment. It is therefore urged that splanchnicectomy be utilized before the hypertension progresses to the Group 4 stage.

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GYNECOLOGIC CARCINOMA IN THE OLDER PATIENT*

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AGE SPECIFIC INCIDENCE

In general, the incidence of cancer increases with age. Figures for the year 1950 from the Connecticut State Department of Health (1) show that the age specific incidence of all forms of cancer rises sharply with advancing age to 1,661.6 cases per 100,000 in women 75 years and older, and 2,616.7 per 100,000 in men in this age group. This incidence in elderly women is nearly twice that found in the seventh decade, three times that of the sixth decade, six times that of the fifth decade, and sixteen times that of the fourth decade (Fig. 1).

In the case of gynecologic cancer this is not so; the age specific incidence falls after the seventh decade. For cancer of the cervix the fall occurs after the fifth decade, for cancer of the uterine corpus after the sixth decade, and for cancer of the ovary after the first part of the eighth decade (Fig. 2).

What relationship, if any, the age specific incidence may bear to etiology is speculative. Some endocrine factor may be involved. Atrophy of the reproductive organs with decreasing hormone levels may militate against the development of carcinoma in old age. On the other hand, the incidence of breast cancer, which might be expected to follow the same pattern, continues to increase with age.

The only exception to the declining incidence of gynecologic cancer with age is carcinoma of the vulva. Carcinoma of the vulva is essentially a skin cancer, and the incidence continues to rise with age in much the same way as with other skin cancers. The 1949–50 incidence figures from Connecticut are too small to be of statistical significance, but in a series of 286 cases of vulvar cancer reported by Berven (2), 60 per cent of the patients were more than 60 years old, and 35 per cent more than 70 years.

In spite of the decrease in the age specific incidence, gynecologic cancer should still be of interest to the geriatrician. Next to breast cancer it is the commonest form of cancer in women. Of 156 primary cases of adenocarcinoma of the uterine corpus seen at Yale Medical Center from 1932 to 1951, 82 per cent were discovered in women past the age of 50, and 51 per cent in those past the age of 60. Of 267 primary cases of epidermoid carcinoma of the cervix in the same period, 53 per cent of the patients were over 50 years of age and 25 per cent were over 60 years.

CANCER IN THE OLDER PATIENT

During the author's two-year association with Yale Medical Center, 53 cases of gynecologic cancer in patients over 65 have been seen. By decades of life and sites of origin the patients were divided as follows:

* Presented before the Graduate Symposium on Geriatric Medicine given by the American Geriatrics Society in New York, N. Y., November 12 and 13, 1954.

** Associate Professor of Gynecology.

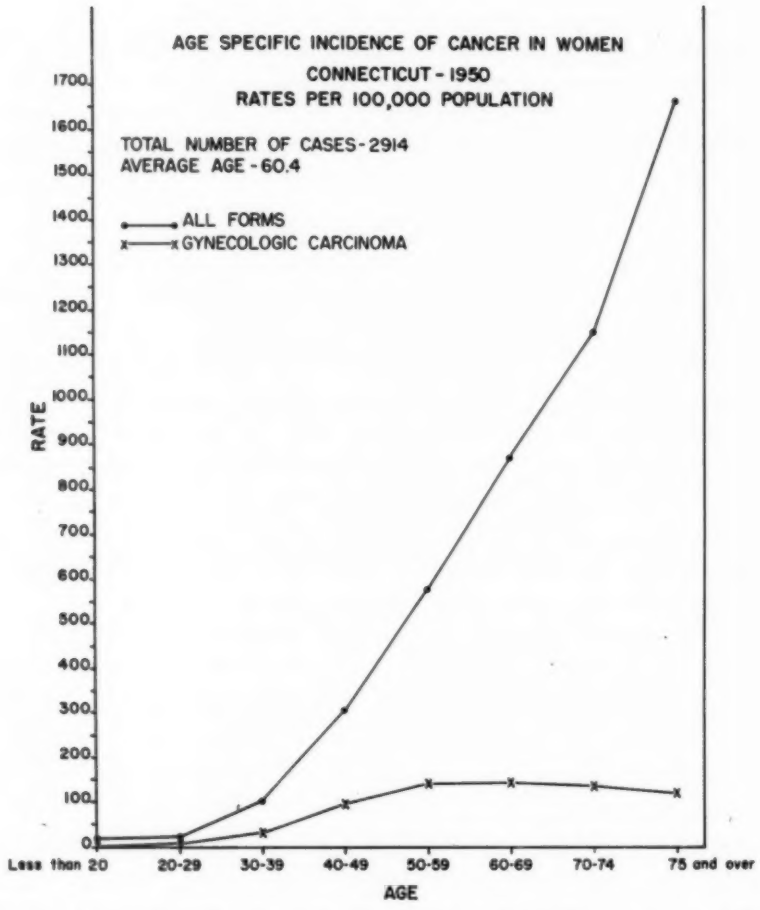

FIG. 1. (Based on statistics from the Connecticut State Department of Health.)

Decade		*Site of Origin*	
Seventh	22	Cervix	21
Eighth	23	Corpus	19
Ninth	6	Ovary	5
Tenth	2	Vagina	4
	—	Other	4
	53		

One would have to be an extraordinary optimist to look forward to a sizable five-year salvage in this group of patients. The number of cases is too small to be of significance; therefore, the 32 patients (60 per cent) who were alive without evidence of disease when last seen will not be discussed, except to note that treatment at least proved palliative and made the declining years of these patients more comfortable. The only significant complication in this group was a ureteral fistula in a patient undergoing partial exenteration for adenocarcinoma of the rectum and cervix. This mutilating type of surgery is not advocated in the older age group unless there is no other acceptable form of treatment.

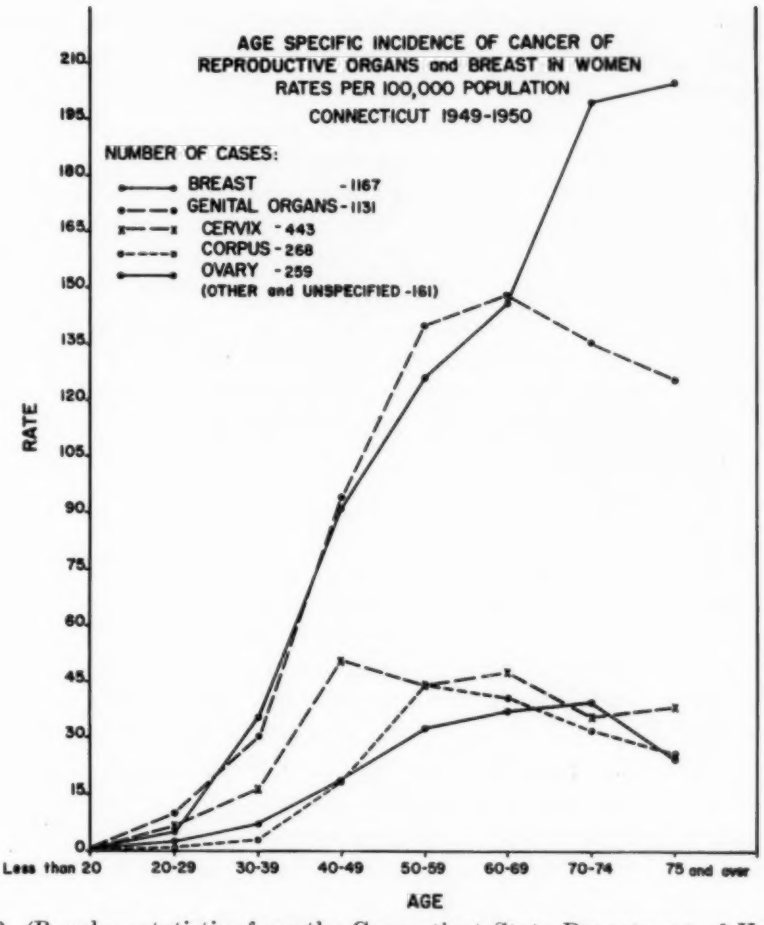

FIG. 2. (Based on statistics from the Connecticut State Department of Health.)

TABLE 1. *Patients 65 or Over with Gynecologic Cancer*

Alive without evidence of disease		32 (60%)
Died [17], or living with residual disease [4]		21 (40%)
Local cure—died of metastases		3 (6%)
Extensive disease present when first seen		16 (30%)
Local	4	
Metastatic	8	
Recurrent	4	
Died of other causes		2 (4%)
Bronchiogenic carcinoma	1	
Syphilitic aortitis (incidental uterine carcinoma at autopsy)	1	

Of more concern are the other patients (40 per cent) who died or who are living with residual disease. This percentage is nearly twice that occurring in a similar group of patients under 60 years of age undergoing treatment during the same period. Table 1 demonstrates that the increased death rate in this series of

older patients was not due to "old age," as only 2 patients died of intercurrent causes. Three-quarters of the deaths and recurrences (16 cases) were in patients whose disease was so extensive when first seen that it was obviously hopeless from the outset.

The extensive nature of the disease in these patients may be the result of upbringing in an era when Victorian reluctance characterized the approach of a gynecologic patient to her physician. There is also an element of neglect. The elderly patient, whose "time is coming" shortly, sometimes tends to ignore any pelvic symptoms and she does not wish to bother her family. In turn, she is neglected to some extent by those about her, and the physician hesitates to overcome her protests and disturb the dignity of age by a thorough physical check-up, especially a pelvic examination. Considering the excellent results that can be obtained in early gynecologic cancer, this inattention seems most unfortunate to say the least.

TREATMENT

The principles of treatment are the same, in general, regardless of age. Cancer is sometimes described as being more benign in the older patient than in the younger, but this is balanced to some degree by the lowered physical reserve of the older patient. The lower reserve accentuates the need for gentleness in treatment—an accent which is sometimes needed in this era of supervoltage radiation and ultraradical surgery. Radiation is used somewhat more frequently in elderly patients because of their inability to tolerate extensive surgical procedures.

Both radiation and surgery have an important place in the treatment of all forms of gynecologic cancer. The only exception is cancer of the vulva, in which radiation has proved somewhat disappointing. For this condition, the generally accepted method of treatment is radical vulvectomy combined with some form of inguinal node or radical groin dissection.

In cancer of the cervix, vagina, endometrium and ovary, there is a good deal of jockeying between the relative values of radiation and surgery, and occasionally some asperity exists between the proponents of each. Both forms of therapy have important roles.

Cancer of the cervix

In comparing radiologic and surgical results in the treatment of cervical cancer, it must be borne in mind that most surgical reports represent a highly selected series of cases. Among the best results in any reported surgical series are those of Meigs (3) in Boston. Using as nearly as possible the same criteria of selection on a large Radiumhemmet series treated by radiotherapy, very similar rates of cure were obtained, as shown in Table 2. Patients 65 years of age or over, those with serious concomitant disease, those weighing more than 220 pounds, and those with persistent fever or badly infected tumors were excluded. The staging is based on clinical rather than surgical findings. Stage II A is used to refer to the earlier Stage II cases without extensive parametrial spread of the disease (Morris and Meigs (4)).

TABLE 2. *Comparison Between Surgical and Radiologic Results in the Treatment of Cervical Cancer*

	STAGE I		STAGE II A	
	No. of cases	Alive and symptom-free at 5 years	No. of cases	Alive and symptom-free at 5 years
J. V. Meigs (3), 1939–1948. Selected cases*	66	54 (81.8%)	34	21 (61.8%)
Radiumhemmet (5), 1936–1945. Unselected cases†	299	207 (69.2%)	537	340 (63.3%)
Radiumhemmet (5), 1936–1945. Selected cases‡	223	180 (80.7%)	343	258 (75.2%)

* Approximately 15 per cent of all cases examined with a view to treatment.
† Constituting 30.3 per cent of all cases examined with a view to treatment.
‡ Constituting 20.5 per cent of all cases examined with a view to treatment.

These figures in no way lessen the tremendous achievements of those who have contributed to the surgical approach to the problem of cervical cancer. They have shown that surgical procedures can be carried out with a low mortality and with a very satisfactory rate of cure.

We employ radiation therapy as our primary method of treatment in cervical carcinoma for the following reasons:

1. The incidence of urinary and other complications appears to be lower with properly administered radiation therapy. The best pelvic surgeons, such as Meigs (3), report an incidence of ureteral fistula of about 7 per cent. Almost all patients have some urinary difficulties. Good radiation therapy should not have a fistula rate of more than about 0.5 per cent (Kottmeier (5)), and should have lower mortality and morbidity rates than those for radical surgery. Furthermore, the vagina is essentially obliterated when an adequate radical operation is performed, whereas it usually remains adequate for intercourse following properly administered radiation therapy.

2. Radical surgical procedures inevitably limit any subsequent radiation therapy, should there be a recurrence. In the absence of the uterus and upper vagina, satisfactory radium application is impossible, and only external therapy is available for the treatment of recurrence—essentially as a palliative measure.

3. Good radiation therapy does not preclude later surgery in the event the tumor is radiation resistant—in fact it may shrink and devitalize a bulky tumor, facilitating its removal.

Radiation is given by a modified Stockholm technique, and if the response to radiation is poor, a radical operation is carried out.

The answer to the choice of method of treatment does not come from comparing separate series or from alternating cases (one treated by radiotherapy and the next by surgery). The real question is which tumor will respond better to surgery and which to radiation. The patients that can be cured by one method are not necessarily the ones that can be cured by the other method.

Significant contributions to the study of radiation sensitivity have been made

TABLE 3. *Cytologic Response to Radiation*
(Cervical and Vaginal Carcinoma)

Response	No. of cases	No. with recurrent disease
Good (75–100%)	17	2 Probable recurrence in pelvic wall (pain—no palpable tumor). 1 Inguinal-node recurrence (treated by radical operation). No local recurrence.
Intermediate (70–74%)	8	3 Died with cancer. No local recurrence.
Poor (0–69%)	23	7 Died with cancer. (5 with local recurrence). 4 Local recurrences (treated by radical operation).
Total	48	10 Died with cancer. 2 Living with recurrence. 36 Living without evidence of disease.

by Graham (6). Although much of this work remains to be substantiated, in a small series of cases of vaginal and cervical carcinomas in which we have been carrying on cytologic-response studies[1] during the past two years, the results have already been of considerable help in indicating good or poor radiation response (Table 3).

We have classified as a good response to radiation all cases in which 75 per cent or more of the cells in the vaginal smear showed a radiation effect (such as swelling, vacuolization or nuclear changes) during treatment. Less than 70 per cent radiation effect was considered a poor response, and the remainder were classed as intermediate. Mrs. Ruth Graham was kind enough to check some of our material and, although our cytologists have not had great experience, it was gratifying to note that the results were correlated closely.

It is incorrect to draw conclusions from such a preliminary evaluation of this work, and it is obvious that the cytologic response alone does not provide the final answer. A "good response" tumor may have distant metastases well beyond the effective limits of radiation. On the other hand, a "poor response" tumor may be so small that the local cauterizing effect of the extremely high doses of radiation received on the surface of the cervix may destroy it in spite of its being resistant. In addition to cases in which tumor was found, we have performed a radical operation on 4 cases in the poor response group and on 1 in the intermediate group, without finding any tumor.

Nonetheless, it is of interest to note that only 3 out of 17 recurrences or deaths occurred in the good response group, and that in none of these was there local recurrence in the cervix or vagina. There were 11 cases of residual or recurrent disease in the poor response group. In all of these the tumor was palpable on pelvic examination. Of 9 cases of residual or local recurrent cancer in the cervix or vagina, all occurred in the poor response group.

[1] Supported by an institutional research grant from the American Cancer Society.

Some of the critics of this investigative program have pointed out that the local recurrence rate is far too high, stating that it should not exceed 2 or 3 per cent. Kottmeier (5) reported that in 32.4 per cent of a series of 2,544 cases receiving full radiation treatment in Stockholm (1936–1945), either the local tumor was not cured by the radiation (643 cases) or there was local recurrence in the cervix or upper vagina after apparent healing (180 cases). Schjött-Rivers (7) reports similar results from Norway. In 718 cases with an apparent cure rate of 45.3 per cent, he found that more than 20 per cent proved to be either locally radiation resistant or later had a local recurrence. These findings furnished justification for his program of carrying out hysterectomy following radiation therapy. Should the Scandinavian results have been poor, these figures could be explained on the basis of poor radiation therapy; but actually the results were considerably better than those reported by some authors claiming lower local recurrence rates.

Cancer of the endometrium

In endometrial carcinoma the value of the combination of radiation therapy and surgery seems to be well accepted. In the 1953 Annual Report edited by Heyman (8), 1,765 cases of corpus cancer treated at institutions favoring primary hysterectomy had a five-year recovery rate of 54.5 per cent; of 2,078 cases treated at institutions favoring primary radiotherapy the five-year recovery rate was 53.5 per cent. The difference between these two figures is insignificant. Nevertheless, there seems to be little question that the combination of the two methods is more effective than either alone, as the following considerations indicate.

It must be remembered that even in the few centers advocating primary radiotherapy, recurrence is treated surgically. As tumor was found at operation in nearly 15 per cent of 990 cases of carcinoma of the corpus primarily treated with radiotherapy in the Radiumhemmet series reported by Kottmeier (9), it seems somewhat unnecessary to wait for the recurrence to manifest itself before performing hysterectomy.

On the other hand, there is no question that preoperative or postoperative radiation greatly diminishes the viability of tumor cells. It would seem that the patient is not being offered the best chance of cure by undergoing operation without it, except in the extremely early or borderline case of endometrial carcinoma. As even normal endometrium may be implanted in a surgical wound (for example, at the time of Caesarean section), the risk of implanting carcinomatous endometrium is considerably greater; this is borne out by the frequency of recurrences at the apex of the vagina in patients receiving no radiation therapy.

In 91 cases of endometrial adenocarcinoma treated at the Grace-New Haven Community Hospital from 1932–1947, the following results tend to substantiate the value of combined treatment:

	No. of cases	*5-Year survivals*
Surgery alone	24	13 (54.2%)
Radiotherapy alone (palliative in 8 cases)	43	14 (32.8%)
Surgery and radiotherapy	24	20 (83.3%)

There is some discussion as to the exact form radiation therapy should take, whether it should precede or follow surgery, and what the time interval should be. We have adopted the Stockholm packing technique, which has given the best results reported for radiotherapy alone, and have been gratified by the number of cases in which no viable carcinoma could be found in the uterus at subsequent hysterectomy. In all but the very poor-risk patients, pelvic node dissection has also been performed. To date, in approximately one quarter of the cases cancerous nodes have been found. This incidence is roughly the same as those reported by Javert (10), Henriksen (11), and Meigs (12). Whether removal of these nodes will produce any significant improvement in the cure rate remains to be seen.

Cancer of the ovary

Ovarian cancer is, in many respects, different from other forms of malignant disease. It is the only known form which at times can be cured when generalized metastases exist. Kottmeier (13) has recently reported the results of 538 cases of ovarian carcinoma. Although he classifies 120 of them as borderline, many in this group had metastases or other evidence of malignancy, and 316 cases were either inoperable, recurrent, or showed incomplete removal of the tumor. Following the use of a combination of radiation therapy and surgery, 36.4 per cent of these patients were alive without evidence of disease at five years. This is an exceptionally good cure rate for cancer of the ovary, and this is the largest series that has been reported.

The method differs from that generally employed in this country, in that the x-ray therapy is given if possible, both before and after surgery, using large ports and low doses in a series of treatments at six-week to twelve-week intervals, modified to suit the individual case. Furthermore, it is considered an error to remove the uterus, which is left for postoperative intrauterine radium insertion. When the uterus has been removed by previous operation, repeated courses of low-dose x-ray therapy through large portals may still be helpful.

In individual cases of ovarian cancer, especially those with metastases, we have employed these methods, which are unorthodox by the usual techniques accepted in this country, with gratifying results. How many permanent cures will be achieved, we cannot say, but the palliative effect is often remarkable.

The following cases are illustrative:

Case I. E.M. (G.N.H.H. # C37504) entered the New Haven Hospital after two previous unsuccessful attempts to remove a papillary adenocarcinoma of the ovary. A biopsy specimen from peritoneal nodules had shown metastases. Ascitic fluid obtained by paracentesis (6,400 cc.) showed adenocarcinoma cells. The tumor mass extended nearly to the umbilicus. A third surgical attempt to remove the tumor was unsuccessful.

The patient was given two courses of x-radiation six weeks apart, using large Stockholm ports, with tumor doses calculated to be 1,480 and 740 r, respectively. The tumor was removed in October 1952, without undue difficulty. There were no metastases except in one node in the mesentery of the sigmoid, which was resected with the specimen. A primary anastomosis was performed. Six weeks later the patient was given a similar course of postoperative x-ray therapy, with a tumor dose of 1,400 r. Since then, the patient has been well without evidence of recurrence.

Case II. M.M. (G.N.H.H. #C32349) was admitted to the New Haven Hospital after two operative procedures to remove a papillary adenocarcinoma of the ovary. A large irregular tumor mass filled the left lower quadrant and part of both adjacent quadrants, and irregular egg-sized tumor masses extended from the umbilicus. Colloidal Au^{198} was given intraperitoneally in an attempt to diminish ascites, without effect. Preoperative x-ray therapy through large ports was advised, followed by resection of the main tumor mass together with the umbilicus and a portion of sigmoid. A course of postoperative x-ray treatment was given. The patient had had a total of 175 abdominal paracenteses, removing up to 8,000 cc. of fluid on each occasion. Although she cannot be considered cured, there has been no need for further paracentesis in the eighteen months since operation.

REQUIREMENTS OF THERAPY

The primary requirement of good radiation therapy is, exactly as in good surgery, to stay within the limitation of tolerance of the patient. Thus, when high injury rates are reported, as in a recent series of 119 cases of cervical carcinoma in which more than half of the patients had serious injuries, this is not an indictment of radiation therapy, but a proclamation of poor treatment.

The second requirement is, within these limits, to give the most satisfactory dose possible which will reduce tumor viability.

Unfortunately, neither of these criteria can be sharply defined in terms of roentgens, milligram-hours, or roentgen equivalents. The effective tumor dose will vary with each tumor and from patient to patient. The limits of tolerance can also be defined only in very general terms. The patient herself must act as a sort of dosage rate meter. This is one reason why good radiation therapy is an art, and so difficult to define. It is perhaps comparable to defining how much sun it takes to acquire a sun tan.

The concept that radiotherapy is essentially a matter of treating space, is incorrect. Merely inflicting a fixed-curve isodose on a patient is almost comparable to making a similar sweep with a scalpel. It is wrong not to recognize the importance of the radiophysicist, but it is equally wrong to turn the patient completely over to his care. The clinician is the one who finally is responsible for the treatment of the patient's disease. The radiotherapist must be primarily a clinician.

Any program, in order to obtain the maximum possible benefits from radiation, must include flexibility and individualization of treatment.

The first factor to be taken into consideration is the problem of over-all tolerance and the general condition of the patient. This must often be built up prior to radiotherapy, exactly as before a major operation, by use of transfusions, vitamins, antibiotics, hormones and other means.

In the presence of *anemia*, radiotherapy loses a significant part of its effectiveness. Oxygen plays a vital role in the biologic effect of radiation, and any loss of the oxygen-carrying capacity of the blood is of extreme importance. *Infection* appears to limit the effect of radiation. Kottmeier (14) found that the cure rate in a series of infected cervical carcinomas was approximately half that of an uninfected group in the same stages. If pelvic inflammatory disease is present, it may show marked exacerbation following radiotherapy. Emphasis has been placed on the importance of removing radium in the presence of any significant rise in temperature—which we consider to be in the neighborhood of 102°F. or

over. In the presence of extreme *cachexia*, radiation must be given with care and obviously caution must be observed in the presence of active *phlebitis*, recent *coronary disease*, *congestive failure*, recent *cerebral accident*, and similar systemic diseases. Age per se, hypertension, diabetes, arteriosclerosis, asthma, emphysema, mild renal impairment, and other disorders of this nature without complicating factors, are not contraindications to treatment. However, in general, we employ radiation doses that are approximately 20 per cent lower in elderly patients.

The second factor of importance concerns the local limitations of tolerance. In radiation therapy in the pelvis, the local limitation centers chiefly around the avoidance of an overdose to rectum, bladder and small bowel. Overdosage has a direct radiation effect on these structures, rather than an indirect effect related to the calculation of a dose to some imaginary point in the pelvis. For this reason, we take direct scintillation-counter readings from bladder and rectum during radium therapy, to supplement calculations which may at times be subject to wide error. A mistake of only a few millimeters in estimating the position of the point involved may result in an error of 100 per cent or more in the dosage. Furthermore, the structures in the pelvis are so elastic that the radium will move considerably in relation to calculation points with shifts in position by the patient or with autonomic movements of bladder or bowel, thus invalidating even a correct calculation. The calculated dose is merely an additional and important guide.

The third important factor is consideration of the nature of the tumor and its anatomic extent. This involves extensive knowledge of oncology, the likely avenues of tumor spread, the radiation sensitivity of various neoplasms, and the alternate surgical procedures available. Among the frequent errors that may be made are incorrect pathologic evaluation of the tumor (especially those of borderline malignancy), a "geographic miss" in administering radiation therapy, the evaluation of operable tumors as inoperable, unwarranted attempts to remove inoperable growths, and the unnecessarily radical removals of tumors that could be treated by less mutiliating measures. As all these factors are based only on empiric observations of patients with tumors, a cancer patient will have a better chance if those who take on the responsibility of treatment have had great experience. This speaks in favor of centralization of treatment in institutions where such experience has been accumulated.

Mutilating surgical or radiation therapy in cancer is justified only if it can be demonstrated that a significantly better cure rate results therefrom.

There are a certain number of patients that can be cured by existing methods of therapy. There is another group that cannot be cured. It is important to avoid injury or death in those that can be cured, and to avoid making life more miserable for those who cannot.

SUMMARY

Unlike the general incidence of cancer, the age specific incidence of cancer of the cervix decreases after the fifth decade, cancer of the corpus after the sixth decade, and cancer of the ovary after the eighth decade.

The principles of treatment are the same, regardless of age. In cancer of the cervix the choice of radiation or surgery is governed by the response of the tumor. In 23 cases with poor cytologic response to radiation there were 9 local recurrences; in 25 cases with good or intermediate response there were no local recurrences. In a series of 91 cases of cancer of the endometrium, those treated with radiation alone showed a 5-year cure rate of 33 per cent; with surgery alone, 54 per cent; but with surgery and radiation, 83 per cent. Combinations of radiation and surgery in ovarian cancer also appear advantageous. The primary requirement of therapy is to stay within the limits of tolerance of the patient and avoid injury.

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Abstracts of Current Literature

SYMPOSIUM SUR LA BIOLOGIE DU VIEILLARD (Symposium on biology of the aged), *Presse méd.* **62:** 765 (May) 1954.

I. Reports

Binet, L. and Bourlière, F.: The physiologic bases of the phenomena of aging.—Senescence and senility are distinct phenomena. The former is a manifestation of the progressive transformations that a human being undergoes during the life cycle, whereas senility is the end-result of this slow evolution and constitutes its terminal stage. Senility is characterized by morphologic and functional involution of tissues and organs. Such involution begins at about age 50 but all tissues do not age at the same rate; this asynchronism may play a part in pathologic processes. While the internal environment remains constant, the adaptability of functions diminishes progressively in the senile subject. All vertebrates do not age in the same way nor with the same rhythm. In rodents, growth can be checked and longevity increased but, to date, not in other carnivores or man. In gerontologic research, results cannot be translated with impunity from rat to man. In man it is not always easy to distinguish in the aged individual the physiologic from the pathologic. Numerous degenerative diseases are favored by a senile terrain but in themselves have nothing to do with physiologic aging. *Delaunay, A.: Aging of connective tissue and intercellular substances.*—Aging in all superior vertebrates is characterized by two more or less constant changes—involution of organs and shrinkage of connective framework. Although the histologic aspects of the changes in connective substance have been known for a long time, no idea of the physiologic aspects existed before 1940. Since then interest has grown in connective tissue, and the application of perfected methods permits determination of the structure of collagen fibrils and demonstration of the existence and analysis, at least grossly, of the chemical structure of the fundamental ground substance. Simultaneously progress has been made in the physiologic domain. Discovery and study of hyaluronidases and collagenases has thrown light on some interactions between hormones and vitamins, on the one hand, and the physiology of connective tissue on the other. Studies that have added to our knowledge of aging of connective tissue and intercellular substances are few. The author believes we shall understand this better when we know what factor conditions the bonds which link polypeptide chains in protofibrils and the protofibrils in the collagenous fibrils, what orients the processes of polymerization and depolymerization in the ground substance, and the exact mechanisms that unite ground substance and collagen devices. Convenient methods of investigation are as yet lacking. Reported are experiments on the action of sodium salicylate in vitro on blood serum, potato starch, milk, collagen A, and egg white. The opalescence and jellifying of blood serum, the swelling and solid gel formation of potato starch, the viscous globule formed by casein, the precipitation of collagen A, and the jellifying of egg white by this substance may all be interpreted as phenomena of polymerization or polycondensation. These studies are of limited significance but it seems reasonable that changes analogous to those seen in vitro may occur in vivo. One day it may be possible to obtain precise evidence of the "life" of the colloidal complex which forms the connective framework, and consequently the fundamental causes of aging. *Panella-Casas; Monteys, J.; Ferrer, D.; Manchon, F., and Hernandez, G.: Senile osteoporosis.*—The concept of, and pathologic processes in senile osteoporosis are reviewed. The disease occurs more frequently in women than in men, the ratio being 5:1. A relationship with protein disequilibrium is probable in the sense of a catabolic modification of the nitrogen balance in the aged. There seems to exist in all osteoporotic processes the same pituitary-adrenal-gonadal modification. The hormonal changes are characterized by a predominance

of catabolic over anabolic hormones in protein equilibrium. In its advanced stage senile osteoporosis has seemed to be irreversible. To be efficacious, treatment should be commenced early and must be prolonged. In general, postmenopausal osteoporosis responds to treatment with estrogens and androgens. Early detection of the osteoporotic process offers the best probability that hormone therapy will be successful. *Laroche, C.: Endocrine glands and senescence.*—In the course of aging, endocrine glands undergo the same pathologic processes as other tissues. This involution varies in intensity among the different glandular tissues. The genital glands age rapidly, especially in the female, whereas other organs such as the anterior pituitary and the adrenal appear to remain in a definitely active state even in the very aged. Thyroidal hypoactivity seems to be linked to an adaptation to reduced bodily requirements rather than to a true hypothyroidism. Adrenal hyperplasia is frequent and occurs at the expense of the zona fasciculata. The excretion of 11-oxysteroids is normal and the adrenal responds to pituitary stimulation. The excretion of androgens is diminished because of involution of the testes and lessened adrenal secretion. This involution is slow and sexual decline depends not only on testicular regression but on the general slackening of physical and psychic functions. The arrest of maturation of spermatozoa is very late. Involution of the ovary is rapid, but hormone determinations and vaginal smears show some follicular activity well after the menopause. Decline of sex hormone secretion has effects on the general metabolism and particularly on the secondary sexual characteristics, the trophicity of the skin and the processes of osseous calcification. The esters of testosterone enable notable amelioration of physical and psychic dysfunctions to be achieved in aged subjects. They elevate the basal metabolism and basal expenditures. Estrogens have a less powerful but significant effect, especially on cutaneous and osseous disturbances. True preventive and curative therapy of senescence consists of the combined administration of small physiologic doses of thyroid, gonadal and adrenal hormones. *Bour, H.: Observations on the lung in the aged.*—Studies on the function of ventilation in 60 women beyond the age of 63 years show that ventilation is considerably disturbed in the aged. Essentially this is because of dissociation between the power of inspiration (which, although diminished, remains good) and the power of expiration (which becomes more altered as greater restoration of pulmonary air is required). These changes elicit a grave disturbance in diffusion of gases and in their intrapulmonary mixture. The ventilatory reserve is also considerably diminished. Thus, if the respiratory function appears to be subnormal at rest, all real effort is practically impossible for the aged subject without causing considerable respiratory difficulty. This loss of power of expiration may result from multiple factors—thoracic, muscular, diaphragmatic or, more properly, pulmonary and bronchovascular sclerosis with emphysemic distension of the lung. Respiratory function is also greatly modified. Although alveolar air appears normally saturated in oxygen, in the elderly a diminution in consumption of oxygen, which averages 173 cubic centimeters, is always noted. Whereas it is necessary for a younger normal subject, to breathe 1.8 to 2.5 liters of air in order to consume 100 cc. of oxygen, in the aged the ventilation ought to be 3.5 liters. Whereas per liter of expired air an adult consumes 60 cc. of oxygen, an aged individual consumes only 30 or 35 cc. Thus, in the aged, increased ventilation is necessary in order to assure moderate tissue respiration. Further research is in progress on the oxyphoric power of the blood and the permeability of the alveolo-capillary membrane, in an effort to understand the mechanism of this dissociation in the aged of the two factors essential for respiration. *Mathé, G.: The blood and internal environment of the aged subject.*—The blood and internal environment of the aged nonpathologic subject differ very little from those of any adult. To be noted are: a tendency to lowering of the number of erythrocytes between the ages of 60 and 95 years (statistically significant); a slight diminution of the metabolism of hemoglobin; a progressive atrophy of lymphoid tissue and volumetric diminution of the red marrow; a distinct increase in capillary resistance; a slight diminution in blood volume; a tendency to lowering of the creatinine level and to elevation of the urea and uric acid levels; a lowering of cholesterol concentration to subnormal values after the age of 60 years; and a frequent decrease in the alkaline reserve and the pH of the

plasma to levels lower than those for adults in general; whereas the levels of calcium and potassium are slightly higher.

II. Communications

Bourguignon, G.; Bourlière, F., and Bourguignon, A.: Muscular fatigue of normal subjects past 50 years of age.—Studies were carried out by the Bourguignon method of tetanizing muscle. In a normal subject of less than 50 years of age no variation in chronaxes is observed. After a normal muscle has performed work by lifting a weight, the chronaxy of the active bundles (small chronaxy) increases and then returns to normal. The degree of fatigue is given by the surface of a triangle, the base of which is the total time of variations, and the height of which is the percentage of the maximal variation. The chronaxy of median bundles does not vary and that of slow bundles varies inversely with that of active bundles. In myasthenic syndromes, simple placing in tension by tetanization, without exterior work, produces the same variations as the induction of fatigue in the normal subject. Over 50 or 55 years of age, with no pathologic cause, a myasthenic syndrome commences. The degree of fatigability does not correspond to the real age of the subject, but to his degree of senility. Thus, though the chronaxes of the muscles at rest do not vary with age (static chronaxy), a characteristic myasthenic syndrome (dynamic chronaxy) appears after the age of 50. *Bourguignon, G., and Bourlière, F.: Vestibular and neuromuscular chronaxes from adult to old age.*—Seventy-nine subjects, 40 women and 39 men, aged 20 to 84 years, were divided into groups by 10-year age periods. The arithmetic mean varied only slightly with age, but the standard deviation increased progressively, beginning with age 60. From a little more than 1 before age 60, it increased progressively up to 3, beginning at age 60. The ratio of the two monoauricular vestibular chronaxes does not vary and is always between 1.10 and 1.20. That which diminishes with age is the number of subjects having chronaxes smaller than 12 to 17 ms at the positive pole. As the smallest chronaxes are those of emotional subjects, their diminution parallels the decrease in emotivity with age, and characterizes "the wisdom of the aged." It also corresponds with the increase in psychomotor reaction time. On the other hand, the neuromuscular chronaxes of 125 subjects aged 20 to 89 years, by 10-year age groups, showed no variation either of the mean or the standard deviation. They are remarkably constant. *Warter, J., Schwartz, J., and Pivel, E.: Adrenal exploration in the aged.*—The authors showed a progressive decrease with age in the rate of urinary elimination of steroids of adrenal origin. They specify an early diminution of excretion of 17-ketosteroids and emphasize that corticoids diminish slowly. By tests with ACTH they could distinguish three types of adrenal response: 1) seemingly normal values initially but a feeble response to adrenocorticotropin, 2) results analogous to those in adrenal insufficiency of pituitary origin, and 3) functional exhaustion of the adrenal.

HORMONBEHANDLUNG NACH RADIKALOPERATION DES MAMMACARCINOMAS (Hormone treatment after a radical operation for breast cancer).
Fikentscher, R. *Med. Klin.* **49:** 1274 (Aug. 6) 1954.

A 56-year-old woman who had menstruated normally up to the time of radical operation for breast carcinoma received androgen as depot Testoviron in doses of 250 mg. for four months and Perandren crystals (100 mg.) for an additional two months, in an attempt to secure hormonal castration. This treatment was expected to prevent recurrences or metastases for a considerable period of time. Hormonal castration with androgens is accomplished through inhibition of gonadotropic function of the pituitary, with resultant suppression of ovarian function. From 300 to 800 mg. of testosterone propionate is required for this purpose and should be administered in doses of 25 mg. three times weekly. With depot forms of androgen in oil the dosage is half as high and the slow absorption corresponds more closely to physiologic conditions. If in inoperable carcinoma, or in case of recurrence or metastases, an anabolic as well as androgenic effect is desired, the dosage of testosterone propionate should be as high as 1,000 mg. per month, continued for three to six months

with reduction to a maintenance dosage thereafter. Systemic and local effects include relief of pain, improvement in well-being, and inhibition of carcinomatous growth and bony metastases. Soft-tissue metastases react poorly and respond better to estrogen. Virilization resulting from high dosage, manifestations of intolerance (such as nausea and vomiting) and psychic phenomena may necessitate a reduction in dosage or the substitution of methylandrostenediol.

ACUTE PEPTIC ULCER AS A COMPLICATION OF MAJOR SURGERY, STRESS, OR TRAUMA.
Fletcher, D. G., and Harkins, H. N. *Surgery* **36:** 212 (Aug.) 1954.

The syndrome of secondary acute peptic ulceration appears to be more common than realized. In a review of 4,102 necropsy records, acute ulceration was found 42 times, an incidence of 1 per cent. Such ulcers may occur following a number of primary conditions including major surgical operations, stress, or trauma. The possible mechanisms of development are discussed. The nature of the primary conditions often includes an element of stress. Therefore a possible mechanism of production of the ulcers involves, as a final pathway, the action of an adrenocortical hormone on the stomach, increasing gastric secretion.

ELECTRORETINOGRAPHIC STUDIES IN ARTERIAL HYPERTENSION. EFFECT OF REDUCTION IN BLOOD PRESSURE ON ELECTRICAL RESPONSE OF HUMAN RETINA.
Henkes, H. E.; van der Kam, J. P., and Sandifort Westhoff, A. J. *A.M.A. Arch. Ophth.* **52:** 221 (Aug.) 1954. 1

Thirty-two patients suffering from arterial hypertension and showing various retina complications were treated with hexamethonium and alkavervir (Veriloid). The effect of a reduction in blood pressure on the electrical response of the retina was investigated. Acute lowering of the blood pressure affected mainly the patients suffering from atherosclerosis of the retinal vessels and general arteriosclerosis. The importance of hypertension for the maintenance of a sufficient retinal metabolism in these cases is stressed. A poor diagnosis in cases of hypertensive retinopathy with/without atherosclerosis is indicated by 1) an electrical response which gains considerably in height after a prolonged stay in the dark of up to 30 minutes; 2) an electrical response which follows an acute fall in blood pressure to the level of 150/90, and 3) an electrical response which shows appreciable variations at different times of recording, although the blood pressure remains approximately constant. (Authors' summary.)

CORTISONE AND NEOSONE IN COMPLICATIONS FOLLOWING CATARACT SURGERY.
Holland, R. W. B., and Lepisto, V. E. *Am. J. Ophth.* **38:** 201 (Aug.) 1954.

A total of 339 patients, who presented some of the common complications following cataract extractions, were treated with cortisone ophthalmic ointment. The patients were observed once a day, then cortisone ointment was applied and the progress was noted. Cortisone and Neosone were found to have a beneficial effect in abolishing the iritis and symptoms associated with the retention of cortex and blood in the anterior chamber (complications of capsulotomy extractions). Postoperative discomfort and hospital stay were shortened by use of cortisone and Neosone. Wound healing did not appear to be affected by the treatment. The drug had no apparent influence on striped keratitis. The therapeutic effect can be produced and maintained by application at 24-hour intervals. (Authors' summary and conclusions.)

THE USE OF CHLORPROMAZINE IN GERIATRICS.
Howell, T. H.; Pinner Harth, J. A., and Dietrich, M. *Practitioner* **173:** 172 (Aug.) 1954.

Chlorpromazine appears to be valuable in geriatric practice and worthy of extended trial. Side effects are rare; drowsiness and unsteadiness of gait can be eliminated by reduc-

tion in dosage. The drug was administered in doses of 25 mg. two or three times daily to a) 20 patients with senile psychosis, b) 10 with emotional reactions, depression, and weeping, c) 19 with pain as a predominant symptom (inoperable carcinoma in 9), and d) 1 with infective jaundice accompanied by vomiting. Forty-three of the 50 patients were benefited, whereas 7 were not. Among the 20 senile psychotic patients, 18 became less restless, agitated and violent. Among the 10 patients with emotional disturbances, 6 improved and became less depressed. Pain was relieved in 18 of the 19 patients with this symptom predominating. They appeared brighter and more cheerful. Some realized that pain existed but were insensitive to it. Vomiting was controlled in the patient with jaundice and in 2 of those with carcinoma of the stomach. The 7 failures were in 4 patients with emotional disturbances, 2 with agitated senile psychosis, and 1 with girdle pains due to tabes dorsalis.

FURTHER OBSERVATIONS ON PATIENTS WITH SEVERE HYPERTENSION SUBJECTED TO ADRENAL RESECTION AND SYMPATHECTOMY.

Jeffers, W. A.; Zintel, H. A.; Hills, A. G.; Hafkenschill, J. H.; Langfield, S. B.; Sellers, A. M., and Wolferth, C. C. *Ann. Int. Med.* **41:** 221 (Aug.) 1954.

This is a review of the clinical course of 125 patients with severe hypertension subjected to adrenal resection (total or subtotal) and sympathectomy (Adson-type) and observed for six months to four years. Twenty-nine (23 per cent) died, more than half of them of a stroke. Adherence to indications and contraindications is imperative. Markedly impaired renal function is the most definite contraindication. Among the 96 survivors, blood pressure responses (as percentages of patients) were: excellent 44, fair 24, poor 12, failure 7. Improvement in electrocardiogram, heart size, and ocular fundi were noted in 37, 34 and 46 per cent, respectively. Relief of congestive heart failure, angina pectoris and headache were noted in 100, 71 and 70 per cent, respectively. Postoperatively, progressive impairment of renal function may occur regardless of the blood pressure response. Unequivocal improvement has not been found. An elevation of the blood urea nitrogen level above 20 mg. per 100 ml. may sometimes be evidence of adrenal rather than renal insufficiency. Fifteen of 57 patients having a subtotal adrenalectomy required no adrenal cortical replacement therapy. Their course did not suggest regeneration of the remaining adrenal fragment. Patients subjected to total adrenalectomy require 20 to 25 mg. of cortisone, 2 mg. of desoxycorticosterone acetate, and 3 to 6 Gm. of sodium chloride daily. A tendency to weight gain is apparent on this regimen. Postoperative sequelae among survivors were: intolerance to cold, 19; mild Raynauds' phenomenon, 18; pigmentation of the skin, 21; and failure of ejaculation in males, 15. Seven of 15 patients showing persistent and marked elevation of blood pressure improved while receiving protoveratrine, hydralazine, or reserpine. Conclusions cannot as yet be drawn from a comparison of the mortality rate among patients subjected to these operations with the rate among patients undergoing throacolumbar sympathectomy. The procedure is as yet an experimental approach.

PROBLEMS OF REHABILITATION IN THE AGED.

Jones, A. C. *Clin. Med.* **61:** 617 (Aug.) 1954.

The technics and philosophy of rehabilitation can accomplish a great deal for the aging patient. Movement is essential for restoration of normal function and has been neglected because of the emphasis on rest. Movement and rest are reciprocal. Extra precautions against exercise or excitement should not prevent the *cardiac invalid*, except for those in class III, from doing useful work. Movement by exercise is the prime factor in the rehabilitation of *hemiplegics*. This begins in bed and proceeds to walking with the aid of appropriate devices and a leg brace. Leg exercises and positioning prevent hip flexion and abduction contractures in elderly persons *minus* one *leg*. Progressive-resistance work for the leg and abdominal muscles assures strength for walking with an artificial limb. Internal fixation of a *fractured hip* is often lifesaving. Exercises for hip, thigh, back and abdominal muscles followed by graded weight-bearing exercises and then walking, enhance the results of

orthopedic surgery after firm pinning of a fracture. Gains in movement, and relief from the pain of *arthritis* can be brought about by movement, traction and heat. Stretching of thickened joint capsules is necessary in the aged as well as in the young. In joints partly immobilized by hypertrophic changes and synovitis, intra-articular injection of hydrocortisone frequently relieves pain and reduces synovial thickening and muscle spasm to such an extent that vigorous physical therapy can restore function nearly to normal. Cortisone or hydrocortisone prepared the patient with *rheumatoid* and *degenerative arthritis* for physical and orthopedic measures. Wooden cylinders furnish an effective means of exercise for crippled hands. Movement in all rehabilitation should begin gradually as conditions permit and be self-assistive insofar as possible. Walking is essential to rehabilitation. Elderly people should assume the upright position and walk if at all possible. Occupational therapy should be directed toward achieving purposeful activity, even gainful employment. Work, properly prescribed, is valuable therapeutically in the management of geriatric and chronically ill patients. The physician can advise and guide in job placement.

OUR GROWING RESPONSIBILITIES TO THE AGED IN OUR MIDST.

Kern, R. A. *Maryland State M. J.* **3:** 393 (Aug.) 1954.

Individuals over age 65 years now comprise 11 per cent of the population over 18 years of age. By 1980 they will comprise 20 per cent. By weight of numbers they claim attention in many fields of endeavor besides medicine, economics, industry, politics and government. The basic economic needs—subsistence, care and treatment—and ways of providing them for the elderly are discussed and advantages and disadvantages pointed out. Keeping the elderly at work protects against lowering the standard of living but, more important, preserves the individual's finest means to happiness. Industry has the responsibility of suiting the activity to the individual, and the physician that of striving to prolong life and preserve vigor of mind and body. In the field of geriatrics, the physician must be alert to changes in structure and function but until more exact information is available on the mechanism of the processes of aging, the prescription of work, rest, diversion and moderation must serve to help the individual achieve his life span in health and happiness. Moderation applies not only to work and rest but also to diet, habits and personal hygiene. The diet must be moderate in quantity and well balanced. Alcohol is permissible in those who have used it previously. Smoking may be allowed, except in the presence of serious cardiac disease. Habits of elimination must be watched. The physician prescribes the mode of life and advises relatives thereon, particularly as to care during illness. As for diagnosis and treatment, attention is called to the possibility of unreliability, the tendency to hide symptoms that would render an elderly individual unemployable, and the frequency of feigned illness. A thorough physical examination and laboratory tests must be the basis for a diagnosis. Perhaps the most useful therapeutic measure is sympathy. The aged eliminate some drugs more slowly and therefore require smaller doses especially of opiates, hypnotics, sedatives and digitalis. The action of some drugs in the elderly may be altered—hyoscyamine, scopolamine, and belladonna at times produce delirium. The unfavorable side effects of ACTH and cortisone are more likely to occur. Broadening experience in surgery in the aged, with better technic, better anesthesia, early ambulation, and the use of antibiotics has furnished some good results in the aged. The prevention of accidents and the correction of deafness should not be overlooked. The keeping of written dated records by the physician is stressed because of their medico-legal importance, as in cases of questioned mental competence.

THE TREATMENT OF INOPERABLE PROSTATIC CARCINOMA WITH Au^{198}.

Orr, L. M.; Campbell, J. L., Jr., and Thomley, M. W. *J. Florida M. A.* **41:** 103 (Aug.) 1954.

Au^{198} is the most suitable radioisotope for use in prostatic carcinoma, because of its stability, its favorable half-life of 2.7 days, the relative uniformity in arrangement of its molecular pattern, its proportions of gamma and beta radiation, and its relatively low cost of production. In determining the dosage of this isotope of gold to be injected interstitially, consideration must be given to distribution of the material throughout the tumor and the

length of time it remains at the site of injection. The problem is to determine maximum and minimum doses in different parts of the injected tissue, as underdosage may result in therapeutic failure, whereas overdosage may decrease the rate of cure and produce undesirable sequelae and complications. Gold does not have a homogeneous distribution so that the radiation must be computed from multiple-point sources of radiation, separated by varying distances. A good or excellent result was obtained in 16 of 26 patients with inoperable prostatic carcinoma treated with Au^{198} by retropubic and perineal instillation. The result was fair or poor in 5, and 5 patients expired. Results improved with improvement in technic, and complications were likewise avoided. Among local changes were softening and shrinking of the carcinomatous area. The chance of early metastasis was minimized by the absorption of beta particles in lymph vessels draining the area. The patients ranged in age from 52 to 81 years. The average size of the prostates was 32 grams. Dosage was based on the size of the gland and the amount of tumor present. The average dose was 90.3 millicuries. Additional Au^{198} could be injected perineally when nodules or areas of hardness developed.

RADIOACTIVE SODIUM CLEARANCE AS A MEASUREMENT OF EFFICACY OF SYMPATHECTOMY IN PERIPHERAL ARTERIAL INSUFFICIENCY.

Reinhard, J. J., Jr., and Dituri, E. *Ann. Surg.* **140:** 67 (July) 1954.

The clearance of radioactive sodium from a lower extremity accurately reflects local tissue circulation in those calf muscles. Increased sodium clearance after sympathetic block and sympathectomy indicates improvement of circulation. Patients with peripheral arteriosclerotic insufficiency have relatively inelastic arteries, with little compensatory mechanism remaining. The sodium clearance and muscle blood flow may be greatly increased by use of sympathectomy in patients with arterial spasm. (Authors' summary and conclusions.)

MORTALITY RATES IN ACUTE MYOCARDIAL INFARCTION. III. THE RELATION OF PATIENT'S AGE TO PROGNOSIS.

Schnur, S. *Ann. Int. Med.* **41:** 294 (Aug.) 1954.

The clinical records of 399 hospital patients admitted with a diagnosis of acute myocardial infarction were reviewed. The degree of illness in each was assessed quantitatively and the patients placed in groups which reflected increasing degrees of severity of illness on admission. These were subdivided into age groups. The principal findings were: (a) Patients who are admitted to the hospital seriously ill are generally older than those who are mildly ill on admission, and this factor primarily accounts for the observation that higher mortality rates are found in groups with higher average age. (b) In patients who are equally ill on admission, a comparison of the mortality rates at various age levels reveals a slightly higher death rate in the older patients, which may possibly be due to the nonspecific progressively increasing death rate associated with advancing age. (c) The patient's age per se is of no value in predicting recovery from this disease in those who enter the hospital mildly or critically ill, is probably of limited value in seriously ill patients, but is of definite value in all those above 75 years of age. (d) In general, the patient's age is a decidedly less important prognostic factor than is the determination of his condition on admission (pathologic index rating), or the appearance during the course of the disease of specific clinical states known to affect prognosis adversely.

VALUE AND DETRIMENT OF SENILE MENTAL CHANGES.

Stoll, W. A. *Schweiz. med. Wchnschr.* **84:** 922 (Aug.) 1954.

Certain qualitative, but not quantitative, similarities exist between normal mental aging and senile dementia as concerns, among other things, diminution in perception and recent recall or the lability of the emotions. The mental changes in senility can exert a positive influence if the personality of the aged person includes a consciousness of reality and an emotional tempering of old age. They are detrimental if the personality is poor in content and stunted. (Author's summary.)

AMERICAN GERIATRICS SOCIETY

THE 1955 ANNUAL MEETING

The 12th Annual Meeting of the American Geriatrics Society will be held at the *Hotel Roosevelt* in *New York City* on *April 21 and 22, 1955.*

The Hotel Roosevelt in New York has set aside a number of rooms to take care of Fellows who plan to attend the meeting. Write to Mr. A. G. Schellenberg, Reservation Manager, Hotel Roosevelt, Madison Avenue at 45th Street, New York 17, N. Y. Mention that you will attend the annual meeting and Mr. Schellenberg will be glad to take care of your needs.

The Scientific Sessions will be held in the Palm Terrace Room.

The Annual Business Meeting will be held in the Palm Terrace Room immediately following the close of the afternoon session on Thursday, April 21.

The Annual Dinner is scheduled for the Palm Terrace Room on Friday evening, April 22, at 8 o'clock preceded by cocktails in the foyer of the Palm Terrace Room at 7 o'clock.

Local Arrangements Committee: Thomas H. McGavack, M.D. (Flower and Fifth Avenue Hospitals, New York), Chairman; Edward B. Allen, M.D.; Harry A. Coveler, M.D.; C. Ward Crampton, M.D.; Cortez Enloe, M.D.; Cornelius P. Rhoads, M.D.; Harry Seneca, M.D.

Norris J. Heckel, M.D.
President

SCIENTIFIC PROGRAM

HOTEL ROOSEVELT

MORNING SESSION—THURSDAY, APRIL 21

Norris J. Heckel, M.D., presiding

8:00 Registration

9:00 Dermatologic Problems in the Aged
Morris Leider, M.D., New York, N. Y.

9:15 Problems Peculiar to Surgery in the Aged—An Analysis of Over 300 Surgical Operations
Arkell M. Vaughn, M.D. and Michael S. White, M.D., Chicago, Illinois

9:30 Diagnosis and Therapy of Migraine
Harold W. Lovell, M.D., New York, N. Y.

9:45 Results of Treatment of Fractures of the Neck of the Femur in the Aged
M. S. Goldstein, M.D., C. L. Beye, M.D., M. Bonfiglio, M.D. and S. E. Ziffren, M.D., Iowa City, Iowa

10:00–10:20 Question Period
10:20–10:30 Recess for Refreshments

Edward Henderson, M.D., presiding

10:30 MANAGEMENT OF BLADDER DYSFUNCTIONS IN THE PARAPLEGIC PATIENT
John Kingsley Lattimer, M.D., New York, N. Y.

10:45 RECENT DEVELOPMENTS IN THE THERAPY OF CHRONIC RESPIRATORY DISEASES
Carl Muschenheim, M.D., New York, N. Y.

Question Period—*Malford W. Thewlis, M.D.*, presiding

11:00–12:45 **PANEL ON DIABETES IN THE AGED**

Moderator:
Laurance W. Kinsell, M.D., Oakland, California
Collaborators:
Howard Root, M.D., Boston, Mass.
Thomas H. McGavack, M.D., New York, N. Y
Irving Graef, M.D., New York, N. Y.
Herbert Pollack, M.D., New York, N. Y.
Beverly C. Smith, M.D., New York, N. Y.
Edward Tolstoi, M.D., New York, N. Y.
Foster Murphy, M.D., Philadelphia, Pa.

12:45 LUNCHEON

AFTERNOON SESSION—THURSDAY, APRIL 21

Richard J. Kraemer, M.D., presiding

1:45 CAUSES AND MANAGEMENT OF POSTMENOPAUSAL UTERINE BLEEDING
J. Donald Woodruff, M.D., Baltimore, Maryland

2:00 PELVIC FINDINGS IN WOMEN AFTER 65
Dean Farley, M.D., and John R. Wolff, M.D., Chicago, Illinois

2:15 CORRELATION OF X-RAY DIFFRACTION AND METAL CONTENT OF AGING AORTA
Hans H. Zinsser, M.D., Los Angeles, California

2:30 TUBE FEEDING IN ELDERLY PATIENTS
James Barron, M.D. and L. S. Fallis, M.D., Detroit, Michigan

2:45 MANAGEMENT OF ANESTHESIA IN THE OLDER AGE GROUP
John E. Osborn, M.D., Rochester, Minnesota

3:00–3:20 Question Period
3:20–3:30 Recess for Refreshments

Edward B. Allen, M.D., presiding

3:30–5:30 **PANEL ON CARDIAC AND CIRCULATORY DISEASES**

Moderator:
C. T. Stone, M.D., Galveston, Texas
Collaborators:
George Griffith, M.D., Los Angeles, California
Hugh Montgomery, M.D., Philadelphia, Pa.
Oglesby Paul, M.D., Chicago, Ill.
Gerald H. Pratt, M.D., New York, N. Y.
Charles Fox, Jr., New York, N.Y.

5:30 **Business Meeting**—Limited to members only.

MORNING SESSION—FRIDAY, APRIL 22

Hollis E. Clow, M.D., presiding

8:00 REGISTRATION
9:00 DIAGNOSIS AND TREATMENT OF CHRONIC GLAUCOMA
William F. Hughes, Jr., M.D., Chicago, Illinois

9:15 THE DILEMMA OF GASTRIC ULCER—BENIGN OR MALIGNANT? A PLAN OF MANAGEMENT FOR GERIATRIC PATIENTS
Brock E. Brush, M.D. and Robert J. Priest, M.D., Detroit, Michigan

9:30 TREATMENT OF INTESTINAL OBSTRUCTION IN THE AGED
Frank Glenn, M.D. and George Wantz, M.D., New York, N. Y.

9:45 CONCERNING THE DIAGNOSIS AND TREATMENT OF SUBDURAL HEMORRHAGE IN THE AGED
Matthew T. Moore, M.D., Philadelphia, Pa.

10:00–10:20 Question Period

10:20–10:30 Recess for Refreshments

Thomas H. McGavack, M.D., presiding

10:30 JAUNDICE IN THE AGED: DIAGNOSTIC AND THERAPEUTIC IMPLICATIONS
Frederick Steigmann, M.D. and V. Godellas, M.D., Chicago, Illinois

10:45 URINARY 17-KETOSTEROID EXCRETION AS INFLUENCED BY AGE AND DISEASE
Thomas H. McGavack and Sidney Pearson, New York, N. Y.

11:00–12:45 **PANEL ON OSTEOPOROSIS**

Moderator:
Ephraim Shorr, M.D., New York, N. Y.

Collaborators:
Daniel Laszlo, M.D., New York, N. Y.
Nathan W. Shock, Ph.D., Baltimore, Md.
G. Donald Whedon, M.D., Bethesda, Md.
Harry L. Jaffe, M.D., New York, N. Y.

12:45–1:45 LUNCHEON

AFTERNOON SESSION—FRIDAY, APRIL 22

Harold G. Wolff, M.D., presiding

1:45 DIAGNOSIS AND TREATMENT OF PAIN IN THE ACROMIO-CLAVICULAR JOINT
Charles V. Heck, M.D. and Fremont A. Chandler, M.D., Chicago, Illinois*

2:00 THE PREFERENCE FOR STREPTODUOCIN IN THE TREATMENT OF TUBERCULOSIS OF THE AGING
Harry Shubin, M.D., Philadelphia, Pa.

2:15 ROENTGEN THERAPY IN CHRONIC CHEST SYMPTOMS IN THE ELDERLY
Anthony F. Rossitto, M.D., Wichita, Kansas

2:30 THE TREATMENT PARKINSON'S DISEASE IN THE AGED
Robert S. Schwab, M.D., Boston, Mass.

Laurance W. Kinsell, M.D., presiding

2:45–4:45 **PANEL ON CANCER**

Moderator:
C. P. Rhoads, M.D., New York, N. Y.

Collaborators:

HORMONAL THERAPY IN CANCER
Rulon W. Rawson, M.D., New York, N. Y.

EVALUATION OF ADRENALECTOMY FOR CANCER OF THE PROSTATE AND BREAST
H. T. Randall, M.D., New York, N. Y.

PALLIATIVE THERAPY OF CANCER OF THE LUNG
D. A. Karnofsky, M.D., New York, N. Y.

THE INDICATIONS FOR THE USE OF ISOTOPES IN MALIGNANT DISEASES
J. E. Rall, M.D., New York, N. Y.

* Deceased, December 24, 1954.

PAPERS READ BY TITLE

TURNING BACK THE CLOCK
Simeon C. Allen, M.D., Boston, Mass.

CONGENITAL HEART DISEASE IN THE AGED
Louis F. Bishop, M.D., New York, N. Y.

ADVANTAGES OF AMBULATORY PROCTOLOGY TECHNIQUES IN THE ELDERLY PATIENT
Alfred J. Cantor, M.D., Long Island, N. Y.

ARTERIOSCLEROSIS AND MODERN LIVING
Aris Carpousis, M.D., Washington, D. C.

CARCINOMA OF THE BREAST IN THE AGED
T. C. Case, M.D., New York, N. Y.

EARLY DIAGNOSIS OF CHRONIC DISEASE. USE OF EMISSION SPECTROSCOPE IN DETERMINATION OF TRACE ELEMENTS IN HUMAN BLOOD
Henry Eisfelder, M.D., Roslyn Heights, N. Y.

THE USE OF DIGITALIS IN THE GERIATRIC PATIENT
Samuel Epstein, M.D., Brooklyn, N. Y.

A GERIATRIC CLINIC IN A GENERAL HOSPITAL—FIRST YEAR'S EXPERIENCE
Louis Friedfeld, M.D., New York, N. Y.

NEWER ASPECTS AND TECHNIQUES IN GERIATRIC PSYCHIATRY
Hal W. Geyer, M.D., Milford, Delaware

ATTITUDE THERAPY FOR NON-INSTITUTIONALIZED ELDERLY PSYCHOTICS
Ralph Ginzberg, M.D., Tomah, Wisconsin

SERUM BETA-LIPOPROTEIN IN THE AGED: METABOLIC CORRELATION
Leo Gitman, M.D., Brooklyn, N. Y.

SHOCK THERAPY FOR THE AGED (INDICATIONS, PROCEDURE AND RESULTS)
Hirsch Loeb Gordon, M.D., New York, N. Y.

THE USE OF DESOXYCORTICOSTERONE ACETATE IN THE TREATMENT OF GASTRIC AND DUODENAL ULCERS
George Joyce Hall, M.D., Sacramento, Calif.

MEDICAL CARE IN THE OLD AGE ASSISTANCE PROGRAM
William Hammond, M.D., Scarsdale, N. Y.

ARRHYTHMIAS OF THE AGED
Raymond Harris, M.D., Albany, N. Y.

HERNIA IN THE AGED
A. H. Iason, M.D., Brooklyn, N. Y.

GALLBLADDER SURGERY IN THE AGED
C. R. Jablonoski, M.D., Cleveland, Ohio

EFFORT, STRESS, AND CORONARY HEART DISEASE
Edmund Jacobson, M.D., Chicago, Illinois

SALIENT FACTORS IN BRIEF PSYCHOTHERAPY WITH PATIENTS IN LATER LIFE
Hans J. Kleinschmidt, M.D., New York, N. Y.

CURE OF BLINDNESS IN THE OLDER AGE GROUP
Arthur Alexander Knapp, M.D., New York, N. Y.

THE MEANING AND IMPORTANCE OF POTASSIUM IN PLASMA DETERMINATION DURING THE FOUR-HOUR GLUCOSE TOLERANCE TEST IN VISCEROPTOSIS WITH FUNCTIONAL HYPERINSULINISM
H. Layzer, M.D., Cleveland, Ohio

REAPPRAISAL OF TODAY'S NUTRITION
W. Coda Martin, M.D., New York, N. Y.

PSYCHOTHERAPY NEEDED IN SENESCENT MARRIED COUPLES (CASE REPORTS AND THEORETICAL SURVEY)
Joseph Meiers, M.D., New York, N. Y.

THE USE OF A CARBONIC ANHYDRASE INHIBITOR IN THE TREATMENT OF HYPERKALIEMIA
Vince Moseley, M.D., Charleston, S. C.

USE OF HYALURONIDASE IN PEYRONIE'S DISEASE
C. L. Mulinger, M.D., Los Angeles, Calif.

MANAGEMENT OF CATARACT
Brittain Ford Payne, M.D., New York, N. Y.

THE USE OF INTRACUTANEOUS AND DEPOT HISTAMINE IN THE TREATMENT OF OSTEOARTHRITIS AND FIBROSITIS
Irving B. Perlstein, M.D., Louisville, Ky.

SENILE MACULAR DEGENERATION OF THE EYES—WITH CASE REPORTS
Louis F. Raymond, M.D., East Orange, N. J.

NEURO-GERIATRICS; ORGANIC AND PHILOSOPHICAL CONCEPTS
Karl Rothschild, M.D., New Brunswick, N. J.

1. THE SIGNIFICANCE OF LONG-STANDING HERNIA TO THE GERIATRIC PATIENT.
2. OCCLUSIVE ARTERIAL GANGRENE IN THE OLDER PATIENT
Martin E. Silverstein, M.D., New York, N. Y.

PREMATURE VASCULAR DEGENERATION IN DIABETES MELLITUS—PATHOGENESIS, AND RELATION TO AGING
Chester Solez, M.D., Narragansett, R. I.

THE ROLE OF THE SOCIAL WORKER IN REHABILITATION IN AN INSTITUTION FOR THE CHRONICALLY ILL
Mrs. Helen K. Weil, Cleveland Heights, Ohio

A SPECIAL INVITATION TO ALL FELLOWS AND MEMBERS OF THE AMERICAN GERIATRICS SOCIETY

Through the kind cooperation of Miss Frances King, Director, the William I. Sirovich Day Center, 203 Second Avenue, New York City, will be open on Saturday morning, April 23, especially to welcome our Members and Fellows to see and study the splendid work that is being done in this center. The center sponsors a cultural and educational program for older people, and although it has been in existence for a matter of only six years it has already won acclaim for its fine work.

The center has succeeded in its endeavor to offer the older men and women a substitute for such factors as the loss of a workday, loss of routine, or loss of companions.

A visit to the center is an inspiring experience and all Fellows and Members are urged to accept Miss King's kind invitation.

POSTGRADUATE COURSE

STRESS AND AGING

Sponsored by

THE AMERICAN COLLEGE OF PHYSICIANS

THE LANKENAU HOSPITAL

Lancester Avenue, West, at City Line

PHILADELPHIA, PA.

April 20, 21, 22 and 23, 1955

Director—Edward L. Bortz, M.D., F.A.C.P.

Associate Directors—Malcolm W. Miller, M.D., F.A.C.P.
Daniel B. Pierson, Jr., M.D., F.A.C.P.

This is a new course on the schedule of the American College of Physicians, emphasizing the effects of stress on the Vascular System, the Digestive Tract, the Nervous System, the Aging Mind, the Chemistry of Growth, and Premature Aging. It will be conducted in a series of symposia and panel discussions. This new field of thought, is organized in a correlated course, with a faculty well qualified by ability and experience to hold the keen interest of the class. The course is scheduled immediately preceding the 36th Annual Session of the College at Philadelphia, April 25–29, thus making it possible for members from all areas to take the course and attend the Session on one journey.

SYMPOSIA—PANEL DISCUSSIONS

		FACULTY
STRESS AND THE VASCULAR SYSTEM	April 20, A.M.	Drs. Nils P. Larsen (Moderator), E. Weiss, C. Riegel, E. S. Nichol & W. M. Yater.
STRESS AND THE DIGESTIVE TRACT	April 20, P.M.	Drs. T. Grier Miller (Moderator), C. M. Jones, W. L. Peltz, S. Zubiran, M. S. Lopusniak & F. J. Inglefinger.
STRESS AND THE NERVOUS SYSTEM	April 21, A.M.	Drs. Frederic H. Leavitt (Moderator), H. C. Solomon, B. J. Alpers, R. Brickner & C. Rupp.
THE AGING MIND	April 21, P.M.	Drs. Lauren H. Smith (Moderator), J. C. Yaskin, F. J. Braceland, J. F. Hughes, A. P. Noyes & K. Appel.
THE CHEMISTRY OF GROWTH	April 22, A.M.	Drs. Stanley P. Reimann (Moderator), A. Keys, S. Weinhouse, J. Stekol, O. McCay & D. B. Dill.
STRESS AND PREMATURE AGING	April 22, P.M.	Drs. Richard A. Kern (Moderator), J. T. Freeman, T. Pomeroy, J. S. L. Browne & H. Selye.
STRESS AND AGING	April 23, A.M.	Drs. George Morris Piersol (Moderator), E. L. Caveny, J. Brozek, E. L. Bortz (Panel: J. S. L. Browne, R. A. Kern, N. P. Larsen, F. H. Leavitt, T. G. Miller, S. P. Reimann, H. Selye & L. H. Smith).